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THE USE OF METARAMINOL
BITARTRATE TO REDUCE THE
SIDE EFFECTS OF ATROPINE

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BELLADONNA alkaloids are widely used clinically as antispasmodics in obstetrics and in preanæsthetic medication. They are also the recognized antidotes for poisoning by anticholinesterases, and could be used prophylactically in individuals exposed to them. However, to be effective for the latter purpose, atropine or its congeners must be given in doses of such magnitude that undesirable side effects such as postural hypotension begin to make their appearance.¹ It was suggested by one of us (C.A.deC.) that a long-acting pressor agent, administered simultaneously with the atropine, might reduce its side effects. In addition, there is evidence that the use of a pressor agent enhances the value of atropine as an antagonist in poisoning by anticholinesterases.²

METHOD

In the present study 123 medical students at the University of Toronto, of whom 13 were females, were used to compare the effect of 1.5 mg. of atropine sulphate injected intramuscularly, with that of the same dose of atropine sulphate injected by the same route in combination with 5 mg. of metaraminol bitartrate‡ (lævo(m-hydrophenyl) aminopropanol). Forty-one students received atropine alone, 41 received atropine plus metaraminol bitartrate, and 41 received an injection of sterile isotonic saline.

The experiment was included as part of the laboratory course in pharmacology, and was designed to familiarize the students with the pharmacological action of the drugs used, and to demonstrate an experimental method in drug evaluation. The participants were divided into groups of three, and each member of the group received an injection from another member, and, in his turn, gave

an injection. Each then observed the effects of the injection he had given upon the recipient, and recorded them, while he himself was the object of similar observations made by another member of his group. In this way each student acted as both subject and observer. They were ignorant of the nature of the injections, which were presented to them in syringes marked by a letter only (A, B, or C), identical in volume (1.5 ml.) and in appearance.

Assessment of the effects of the injections was made by both physiological and psychological methods. In the former the blood pressure, pulse rate, respiratory rate and pupil size were measured. For the latter, visual and time perception tests were used.

The visual perception test (Mackworth) entails writing down in their proper sequence a group of three letters flashed for 1/16 second each on a screen, 1/16 second apart. By reason of the after-image, each letter appears on the retina about 1/8 second. The test comprises 68 such groups in all, with a ten-second interval between groups. The subjects were tested in this way before the injections, and again approximately one hour after injection. Some improvement in this test is to be expected with repetition, owing to the subject's increased experience. Time perception was tested using the method of positive feedback.³ In this test, a light is displayed to the subject for a given length of time and, as soon as the light goes out, he is instructed to switch it on again for what he judges to be the same length of time. The light is then displayed to him a second time, but on this occasion its duration is made the same as that judged by the student to be equal to the first display. This sequence is repeated a number of times, with the effect that any error on the part of the subject accumulates. He is forbidden to judge time intervals by counting. Fifty-two subjects underwent this latter test, 16 of whom had received atropine alone, 18 the combination of atropine and metaraminol, and 18 isotonic saline.

When the initial visual perception test had been completed, the subjects took their places in the laboratory and sat quietly for five minutes. At the end of this time each subject recorded the blood pressure, pulse rate, respiration rate and pupil size of another member of his group of three, after which the injections were given.

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‡Aramine bitartrate (Merck, Sharp and Dohme).

After the injection the heart rate was charted at half-minute intervals for the first five minutes. Thereafter, this and the other physiological measurements were made every ten minutes, for a period of one hour. The subjects were not permitted to eat, drink, smoke or move about the room during the experiment, while at some time during this hour a proportion of the subjects were chosen at random to take the time perception test.

Finally, the subjects were again tested with the same visual perception film.

RESULTS

Blood Pressure and Pulse Pressure

Injection of atropine sulphate caused the systolic blood pressure to fall, while the diastolic pressure was unaffected (Table I and Fig. 1). The net result was a reduction in pulse pressure (Fig. 2).

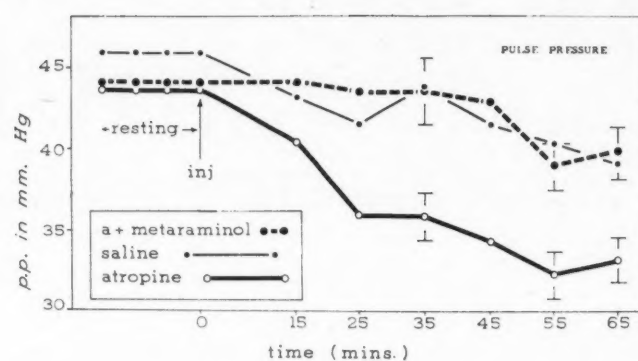


Fig. 2.—Mean pulse pressure following the intramuscular injection of (a) atropine in combination with metaraminol; (b) isotonic saline; and (c) atropine alone. Vertical bars indicate the standard error.

the first half hour, as the effect of the metaraminol wore off, the systolic pressure fell, with a consequent reduction in pulse pressure (Table I and Figs. 1 and 2).

TABLE I.—MEAN BLOOD AND PULSE PRESSURE IN MM. HG AFTER ATROPINE PLUS METARAMINOL, SALINE, OR ATROPINE

		(Time in Minutes)						
(123 subjects)		Resting	15	25	35	45	55	65
SYST.	A. + M.	115.5	118.4	122.3	120.4	117.6	114.5	113.6
	Saline	116.4	112.4	111.5	111.8	110.6	109.2	110.6
	Atropine	115.4	113.4	109.3	106.6	105.8	106.1	107.0
DIAST.	A. + M.	70.8	74.1	78.3	76.9	75.6	75.1	74.4
	Saline	70.7	69.2	70.3	68.3	69.6	68.5	70.1
	Atropine	72.0	72.7	73.0	70.9	71.8	73.6	74.3
P. P.	A. + M.	44.0	44.0	43.4	43.5	42.8	38.9	39.7
	Saline	45.9	43.2	41.5	43.7	41.4	40.3	39.1
	Atropine	43.5	40.3	35.9	35.8	34.3	32.2	33.1

Injection of atropine sulphate plus metaraminol bitartrate caused both the systolic and diastolic pressure to rise by an equal amount so that the pulse pressure remained unchanged. However, after

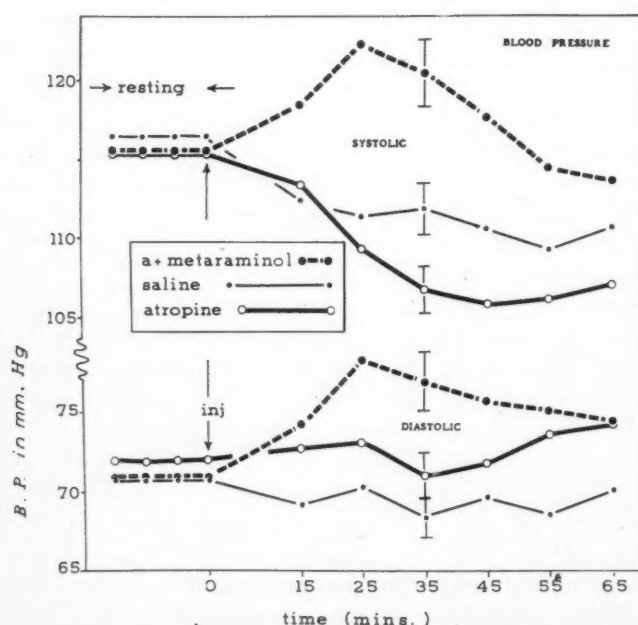


Fig. 1.—Mean systolic and diastolic blood pressure following the intramuscular injection of (a) atropine in combination with metaraminol; (b) isotonic saline; and (c) atropine alone. Vertical bars indicate standard error.

The control subjects receiving saline showed a slow fall in systolic pressure during the observation period but to a lesser degree than in subjects receiving atropine (Table I and Fig. 1). The diastolic pressure was unchanged. The higher systolic pressure observed at the beginning of the test period in the control group was probably related to apprehension.

Heart Rate

Following injection of atropine there was a slight initial slowing of the heart rate from a resting mean of 85 to a mean rate of 83, after which the rate increased to reach a mean peak rate of 105 roughly 35 minutes later, at which level it remained (Table II and Fig. 3). With a combination of atropine and metaraminol bitartrate the initial slowing was both longer in duration and more pronounced (from a mean resting rate of 86 to a mean rate of 75) and the mean maximum rate reached was 95 beats per minute (Table II and Fig. 3), that is, 10 beats per minute less than with atropine alone. In the group which received saline there was a reduction in pulse rate amounting to roughly 5 beats per minute.

TABLE II.—MEAN HEART RATE (BEATS PER MINUTE) AFTER ATROPINE PLUS METARAMINOL, SALINE, OR ATROPINE

(123 subjects)	Resting	(Time in minutes after injection)										
		1	2	3	4	5	15	25	35	45	55	65
A. + M.....	82.5	79.0	75.9	75.9	75.4	75.1	75.1	86.2	94.3	95.3	96.6	98.0
Saline.....	85.9	82.5	83.1	83.3	83.1	83.1	83.5	81.9	82.7	81.1	80.2	81.5
Atropine.....	85.1	84.0	83.2	82.9	82.7	82.8	88.4	100.0	106.3	106.4	106.8	107.1

Respiration

Both atropine alone and atropine plus metaraminol caused a slight increase in respiratory rate in the first 15 minutes after injection. With atropine alone the respiration rate fell during the next 10 minutes to below the rate recorded before injection, following which there was a considerable increase, the rate reaching a maximum 55 minutes

that the changes observed were of doubtful significance.

Eye Changes

Pupillary dilatation occurred with both drugs but to a greater extent with the atropine than with the atropine plus metaraminol combination (an increase in mean diameter of 0.9 mm. compared with 0.7 mm. (Fig. 4)). There was no change in pupil size with the saline injection.

Four subjects who received atropine alone, and four subjects who received atropine plus metaraminol bitartrate, complained of loss of accommodation.

Perceptual Tests

The results on the Mackworth Three Letter Test were scored on the basis of an expected improvement, due to learning, between the run before injection and the run after it. In summary, the results are as follows. Of the 41 students who received saline 24 (58%) showed an improved performance on the second test, of the 40 who received atropine 15 (37%) improved, and of the 39 who received atropine plus metaraminol bitartrate 18 (46%) improved. In short, the performance was better with the metaraminol combination than with the atropine alone, although the figures just fail to reach the 5% level of significance. The greatest improvement in performance was seen in the saline control group.

In the time estimation test, responses are grouped into one of three types, those giving a consistently shorter response, those giving an irregular response, and those giving a consistently longer response. The 52 students tested were evenly distributed among these groups and there was no correlation with the injection received.

DISCUSSION

The experiments reported here show that some, but not all, of the side effects of atropine can be rendered less severe, or obviated, by giving the drug in combination with metaraminol bitartrate. They show that tachycardia is lessened thereby, and the fall in systolic blood pressure and pulse pressure, which is observed after a dose of atropine of this size, is prevented. It is therefore possible that giving metaraminol along with atropine would tend to reduce the incidence of postural hypotension.

Atropine alone caused elevation in heart rate and a fall in systolic arterial pressure and in pulse

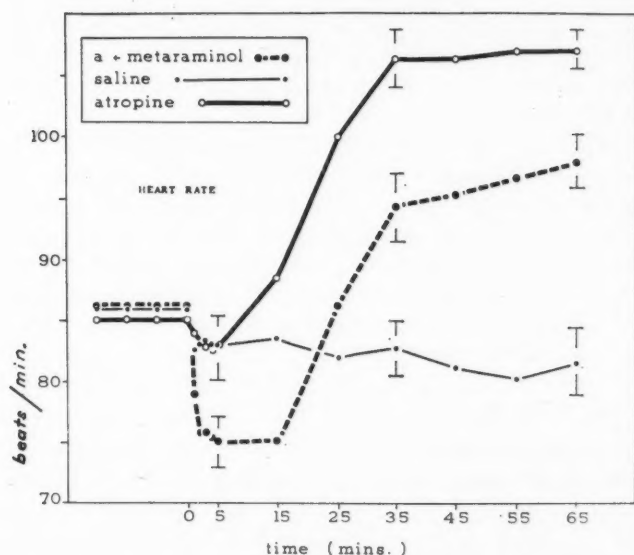


Fig. 3.—Mean heart rate following (a) atropine plus metaraminol; (b) isotonic saline; and (c) atropine alone. Vertical bars indicate the standard error.

after injection. No such increase was observed after the injection of atropine plus metaraminol. On the contrary, after the initial slight increase noted above, the rate fell slowly to reach the pre-injection value after 40 minutes. In spite of these changes in the mean, statistical analysis showed

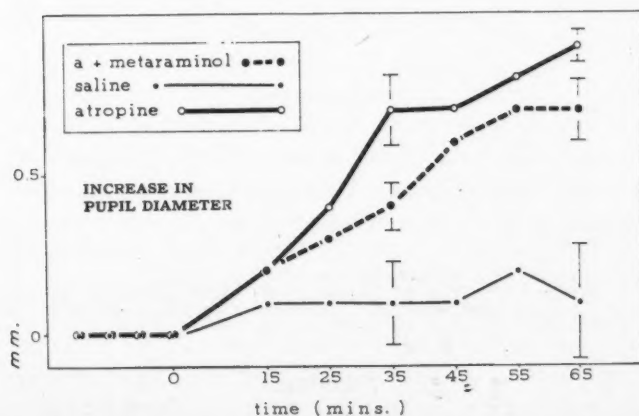


Fig. 4.—Change in mean pupil diameter following (a) atropine plus metaraminol; (b) isotonic saline; and (c) atropine alone. Vertical bars indicate the standard error.

pressure. Tachycardia is attributable to blocking of the vagal supply to the heart, while the usual explanation of the fall in blood pressure after administration of atropine is that it is due to vascular pooling, though the mechanism is doubtful.⁴ However, the present finding that the systolic pressure fell while the diastolic pressure did not, suggests that a fall in cardiac output took place, and this would be in keeping either with a fall in the circulating blood volume or with the known depressant ("negative inotropic") effect that atropine has on heart muscle.⁷

Metaraminol alone produces bradycardia both in human subjects⁶ and in the dog.⁸ Its vasopressor effect is small in normal dogs but is marked in vagotomized or hypovolaemic animals. The same authors found that metaraminol produced a sustained increase in myocardial contractility ("positive inotropic effect"), the coronary flow per unit of work being unchanged. The possibility therefore exists that the modification of the atropine effect brought about by metaraminol in these experiments (namely, absence of any fall in systolic blood pressure) was due, at least in part, to actions on the heart itself.

The experiments also show that pupillary dilatation is less when metaraminol bitartrate is combined with atropine. On the other hand, difficulty in focusing the eyes appeared to occur equally often whether atropine was given alone or in combination with metaraminol, and only a marginal difference in performance was detectable in tests used to evaluate mental concentration.

Although metaraminol bitartrate has a prolonged action in comparison with other pressor drugs (20 to 60 minutes when given intramuscularly), it is not to be compared in this respect with atropine itself, and consequently any modifying effect that an initial dose of metaraminol bitartrate may exert upon the action of atropine must be sought early on. It may be that the three letter visual perception test would have shown a significant difference had it been repeated earlier.

As might be expected, the initial stage of bradycardia which occurs when atropine is injected intramuscularly^{5, 7} was intensified and prolonged by giving metaraminol bitartrate simultaneously with the atropine (Table II and Fig. 3). Presumably the stimulant effect which atropine has on the cardio-inhibitory centre was reinforced by baroreceptor stimulation due to the rise in blood pressure induced by metaraminol. The possibility must be considered that metaraminol, when given as it was here in a single injection together with atropine, decreases the rate of absorption of atropine by a vasoconstrictive action, and that some or all of the changes were due to this. The present experiments do not exclude this possibility, but the fact that all the modifying effects observed were still present as long as one hour later suggests that this is not the whole explanation.

Administration of atropine in doses of this size, or even larger, is indicated in poisoning by anticholinesterases (for example, by certain insecticides and by the nerve gases), and reduction of unwanted side effects would itself justify the administration of a second drug along with it, even if the second drug did nothing to increase the antagonistic potency of atropine. Not only is metaraminol bitartrate effective in reducing side effects but there is suggestive evidence² that it enhances the antagonistic effect of atropine against anticholinesterases.

SUMMARY

The effect of 1.5 mg. of atropine sulphate intramuscularly upon blood pressure, pulse rate, respiration rate, pupil size, power of accommodation, and perception, was compared with that of the same dose of atropine sulphate given in combination with 5 mg. of metaraminol bitartrate, using 123 medical students as subjects. A control series was also done in which sterile isotonic saline was injected.

Addition of metaraminol bitartrate resulted in a significantly higher mean systolic blood pressure, a larger pulse pressure and slower heart rate during the hour following administration, than when atropine was given alone. Pupillary dilatation was also less.

One perceptual test showed a difference in favour of the two-drug combination but the difference was not of significance at the 5% level.

ADDENDUM

The results reported here were obtained with "unrestrained" subjects. There is evidence that in subjects who are lying inactive and are tilted passively, somewhat higher doses of atropine may produce a labile condition of the circulation, some of the effects of which are accentuated by metaraminol.

This might offer some danger clinically and is an example of one of the unexpected hazards which sometimes attend the use of combinations of potent drugs.

The authors wish to express their appreciation to the medical students whose enthusiastic participation made the study possible. The work was a co-operative effort between the Department of Pharmacology, University of Toronto, and the Defence Research Medical Laboratories in Toronto (Project Number D52-20-50-09).

The illustrations were prepared by Mrs. Mary Murphy. Professor D. B. W. Reid advised and assisted in the statistical evaluation of results. This help is gratefully acknowledged.

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RÉSUMÉ

Les alcaloïdes de la belladone sont couramment employés comme antispasmodiques et comme médication préparatoire à l'anesthésie. Ils sont également reconnus comme antidotes

dans l'intoxication par les anticholinestérases. Cependant l'atropine et ses dérivés ne peuvent donner tout leur rendement qu'à condition d'être administrés en doses suffisantes qui malheureusement comportent des effets secondaires indésirables. Les auteurs de cet article ont cherché à contrecarrer ces effets par l'administration simultanée d'un vasopresseur à longue durée. On donna 1.5 mg. de sulfate d'atropine par voie intramusculaire à 41 étudiants en médecine; les variations de tension artérielle, du pouls, de la respiration, de la dilatation pupillaire, du pouvoir d'accommodation et de la perception mentale furent comparées

à celles que l'on observa lorsque la même dose de sulfate d'atropine fut administrée en combinaison avec 5 mg. de bitartrate de métaraminol. On a également étudié une série de témoins qui n'avaient reçu qu'une solution stérile de sérum physiologique. L'addition de métaraminol a causée une élévation importante de la tension artérielle systolique et de la différentielle ainsi qu'une bradycardie dans l'heure qui suivit son administration. L'épreuve de perception intellectuelle a montré une légère amélioration lorsque le métaraminol fut ajouté à l'atropine mais cette différence ne possédait pas d'importance au niveau de 5%.

GERIATRIC PSYCHIATRIC PATIENTS IN GENERAL HOSPITAL AND MENTAL HOSPITAL

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TO THE medical profession as a whole there are two main types of psychiatric facility available for the active treatment of their psychiatric geriatric patients. The first is connected with the larger general hospitals and consists usually of a 25-50 bed unit separated from the medical wards of the hospital. The other type, connected with the mental hospital, is a ward set aside for geriatric patients or perhaps even a separate geriatric building with capacities ranging from 15-20% of the total beds available. This study is an attempt at comparison of the patients admitted to two such institutions and the long-term results of their disease and treatment.

Such a comparison, it is hoped, will produce a twofold result, *viz.*, enable us to show the extent to which these facilities can be employed, and by a study of the problems and results achieved enable us to make some recommendations for their effective use.

METHOD OF STUDY

The particular units chosen for this study are a 33-bed psychiatric unit in a general hospital and a 1500-bed mental hospital. Both are in the southern half of Saskatchewan and draw their patients from an area which has a population of some 450,000. Another general hospital unit of about 30 beds is the only other psychiatric in-patient facility conveniently available for this district.

These two units admitted a total of 191 geriatric patients during the period of the study, January-December, 1957. Fifty-four were admitted to the general hospital and 137 to the mental hospital. Transfers from other psychiatric institutions in the province or patients retaken from a mental hospital parole were not included in this total, but readmissions were.

It should be noted, however, that there is a slight overlap in the two facilities. Five patients (two men and three women) were admitted to mental hospital after having been treated in the psychiatric unit. No special attention was paid to this in the assessment of the study because of the small numbers involved.

This study is in natural sequence to one made at a general hospital psychiatric unit alone that reported the facilities available and results achieved with geriatric patients.¹

The findings reported in the previous study were freely abstracted for our purposes to serve as the basis of comparison with the mental hospital, so that it was then only necessary to search the mental hospital records and obtain information identical with that of the earlier study. Thus a general picture of all the geriatric patients was obtained. These findings, which are listed in Table I, give us information on mean age and range, sex, diagnosis and mean length of stay.

To allow a statistical study of the findings it was decided to group the diagnostic material into broad clinical groupings corresponding as closely as possible to the previous study. Thus five groupings were made which included affective, psychoneurotic, organic, schizophrenic and an additional one made necessary by the presence in mental hospital of another class of patients: those suffering from senility and physical disease alone, with only a vague or controversial psychiatric diagnosis offered. The grouping, delirium, used in the previous study was not found to be satisfactory, as the mental hospital records did not make a clear distinction among the three groups, organic disease, delirium and physical disease (admittedly a more usual classification).

The results of treatment were then studied under the headings used in Table II. A more detailed review was not thought necessary because it rapidly became apparent that to achieve the purpose of the study it was only necessary to have a general knowledge of the particular treatments used. The results achieved were mainly a function of the disease process present, and only minor variations in them were dependent on specific therapy.

When these preliminary surveys were completed, a follow-up study of all surviving patients was made. For a fairly large number this was a simple

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TABLE I.—GENERAL CHARACTERISTICS

		<i>Affective</i>	<i>Psycho- neurotic</i>	<i>Organic</i>	<i>Schizo- phrenic</i>	<i>Sen. and phys.</i>	<i>Total</i>
<i>General hospital patients</i>	Mean age (and range)	66 (60-74)	65 (60-76)	72 (61-87)	63 (62 and 64)	—	67 (60-87)
	Sex	11m-13f	6m-6f	7m-9f	0m-2f	—	24m-30f
	Diagnosis	24 (45%)	12 (22%)	15 (27%)	2 (4%)	1 (2%)	54 (100%)
	Length of stay (and range)	35 (14-71)	29 (11-66)	13 (1-70)	19 (2-36)	—	29 (1-71)
<i>Mental hospital patients</i>	Mean age (and range)	68 (60-82)	66 (62-70)	77 (61-93)	68 (60-81)	77 (63-91)	73 (60-93)
	Sex	12m-17f	4m-5f	44m-16f	5m-8f	12m-14f	77m-60f
	Diagnosis	29 (21%)	9 (7%)	60 (42%)	13 (10%)	26 (20%)	137 (100%)
	Length of stay (and range)	98 (4-322)	36 (17-64)	103 (10-265)	87 (19-123)	84 (7-340)	88 (4-340)

matter, since they remained in hospital or in close contact with a psychiatrist who was available for comment on their progress. To the remainder a simple questionnaire was directed. Again it was necessary to issue a second questionnaire to those who failed to respond to the first, and in this manner over 90% of the original sample were contacted. The results are listed in Table III.

Finally, when the results had been tabulated it was possible to make a statistical survey. In particular, attention was directed to any possible

portionately large number of senile and physically ill persons reported in the Saskatchewan group as noted in Table IV.

Again, when the Saskatchewan group was divided according to treatment facility, this difference remained apparent. In fact, it was even more noticeable since there was only one person clearly labelled under this group in the psychiatric unit and is so listed in Table I.

In addition, there was a significantly greater number of male patients with affective diseases

TABLE II.—CONDITION ON DISCHARGE—1957

		<i>Out of hospital</i>	<i>Remaining</i>	<i>Dead</i>	<i>Not traced</i>
<i>Psychiatric unit</i>	Male n-24.....	24 (100%)	—	—	—
	Female n-30.....	29 (97%)	—	1 (3%)	—
	Total n-54.....	53 (98%)	—	1 (2%)	—
<i>Mental hospital</i>	Male n-77.....	29 (39%)	12 (15%)	36 (46%)	—
	Female n-60.....	33 (55%)	13 (22%)	12 (20%)	2 (3%)
	Total n-137.....	62 (45%)	25 (18%)	48 (35%)	2 (2%)

difference between the total Saskatchewan sample and that of Canada as a whole. For this purpose Dominion statistics bearing on the problem were used.² The inter-relation between the two types of facility was then studied, the basis for the evaluation being possible differences in diagnostic categories, results at the time of discharge, and the status at the time of follow-up. The Chi-square technique was employed, using all five diagnostic categories in the classification table.

RESULTS

In comparing the Saskatchewan sample with that for Canada as a whole it rapidly became apparent that there was a markedly significant difference between the groups. The greater part of this difference was due to the presence of a dispro-

admitted to the general hospital and a presumably complementing difference in the number of male patients with organic disease admitted to the mental hospital.

Considering the groups by improvement great enough to warrant discharge, a significant difference is shown (98% of the psychiatric unit but only 45% of the mental hospital sample).

Further, when the death rate is considered, a very significant difference is demonstrable between the male and female portions of the Saskatchewan group as a whole. Subdividing this group by sex and treatment facility, it is seen that the factor responsible is the greater number of deaths of the males admitted to mental hospital.

Finally, studying the results of the questionnaire to determine any differences in present status (con-

TABLE III.—CONDITION AT FOLLOW-UP—1959

		<i>Out of hospital</i>	<i>Remaining or readmitted</i>	<i>Dead</i>	<i>Not traced</i>
<i>Psychiatric unit</i>	Male n-24.....	13 (55%)	3 (12%)	6 (25%)	2 (8%)
	Female n-30.....	12 (40%)	9 (30%)	3 (10%)	6 (20%)
	Total n-54.....	25 (46%)	12 (23%)	9 (16%)	8 (15%)
<i>Mental hospital</i>	Male n-77.....	17 (23%)	17 (22%)	39 (50%)	4 (5%)
	Female n-60.....	20 (33%)	23 (38%)	14 (24%)	3 (5%)
	Total n-137.....	37 (27%)	40 (29%)	53 (39%)	7 (5%)

TABLE IV.—SASKATCHEWAN AND CANADA COMPARED BY DIAGNOSTIC GROUPS

		Affective	Psycho- neurotic	Organic	Schizo- phrenic	Sen. and phys.	Total
Saskatchewan	Male n-101	23 (23%)	10 (10%)	51 (51%)	5 (5%)	12 (12%)	101 (100%)
	Female n-90	30 (33%)	11 (12%)	25 (28%)	10 (11%)	14 (16%)	90 (100%)
Canada	Male n-3311	812 (25%)	548 (17%)	1568 (47%)	141 (4%)	105 (3%)	3174 (96%)
							other psychoses 4%
	Female n-3030	1126 (37%)	231 (8%)	1307 (43%)	186 (6%)	73 (2%)	2923 (96%)
							other psychoses 4%

sidering only the classifications—out of hospital, in hospital, and dead), another significant difference between the male patients is observed. The males admitted to the psychiatric unit seem better able to keep out of hospital. The liability for this is apparently divided between the remaining two groups—in hospital and dead; that is, neither one accounts for the difference in a significant manner. Considering the latter separately (a less valid technique statistically), there then appears to be a significant difference in favour of the men admitted to general hospital.

DISCUSSION

This study again brings to view many of the difficulties which have been noted in the care of the older psychiatric patient. The first problem, of course, must be one of diagnosis. Certainly the early recognition and treatment of physical disease as distinct from definite psychiatric syndromes, as seen in the disproportion between the statistics of our particular mental hospital and those for Canada as a whole, is a helpful step. However, in spite of the vigorous treatment given these unfortunate people by the admitting mental hospital, they still die—even more precipitously than their fellow psychiatric patients. They only serve to establish the correctness of the contention of those treating them, that they do not belong in the mental hospital but in a hospital more suited for the treatment of medical diseases.³ The same seems to be true for even many of those who enter hospital diagnosed validly as predominantly psychiatric — they do poorly and seem only to have been rudely torn from their homes and brought to the mental hospital to die.⁴

Aside from the difficulty of separating the predominantly psychiatric from the physically ill, there is an added difficulty in the lack of a proper definition for the psychiatric syndromes which appear. In our study we have grouped the separate diagnoses, arteriosclerotic and senile psychoses, under the common heading of organic psychoses. The justification is, of course, that in most cases any other clinical diagnosis is impossible because of a liberal admixture of symptoms of both illnesses (if indeed two illnesses really exist).

The presence of large numbers of such organic mental illnesses in the geriatric population at times leads the unwary or rushed examiner into consider-

ing any old person with obvious mental symptoms as psychotic (and organic). The fallacy of such a conclusion is obvious from the figures presented from both facilities. There is a large percentage of non-organic conditions that respond well to treatment and bear a good prognosis.

Among those who improve in hospital and are discharged there appears the problem of maintaining improvement. Of those people, the male mental hospital patient shows a poor ability to remain out of hospital, as has been demonstrated. The females, on the other hand, show their overall ability to do better than males in survival and prognosis. This is not surprising because it is well known that the female is better equipped to last past the male life span in emotional and psychiatric aspects, as well as in general health patterns.⁵

Considering the groups as a whole, one remarkable aspect is the low number of previous admissions, i.e. the geriatric group seem to have postponed their emotional difficulties by the use of potent defences, and only the relentless stresses of old age (physical and mental) cause them to become ill.

Finally, the important finding in the present study (one noted previously) is the high number of initial mental hospital patients who remain in hospital at the time of follow-up and thus obviously in poor mental health. It is less obvious that they are in fair or good physical condition. Those who had a physical condition precipitating their psychosis are dead; the remainder are dependent on institutional care probably for the rest of their lives. This position makes them a real problem in mental hospital, since they require only custodial care. To give them this care requires extensive if not elaborate facilities, and probably it is for these people that most of the planning with respect to geriatric patients should be directed. Is it better for them and for the mental hospital that they remain there, or are separate facilities indicated?

SUMMARY

A comparison is made between two groups of geriatric psychiatric patients admitted to a general hospital psychiatric unit and a provincial mental hospital respectively during the year 1957. A survey of their general characteristics such as age, sex, diagnosis and length of stay was first made. The results of treatment were then tabulated, both for the time of discharge and at a follow-up time in mid-1959. A statistical

study was then performed to determine if valid differences existed between the two groups. The Chi-square method was the technique employed. A discussion follows which emphasizes the problems of diagnosis and the inevitability, under the present arrangements, of misdirection in the placement of the older person seeking psychiatric help, as well as some of the difficulties inherent in a steadily increasing geriatric population in mental hospitals.

We would like to thank Dr. Humphry Osmond for reviewing the article and for his permission to publish, and Dr. Robert Sommers for his assistance in the statistical evaluation and review.

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RÉSUMÉ

On a établi une comparaison entre deux groupes de malades gériatriques en traitement psychiatrique dont l'un avait été admis au département psychiatrique d'un hôpital général et l'autre à un hôpital provincial pour malades mentaux au cours de 1957. On a d'abord tenu compte de l'âge, du sexe, du diagnostic et de la durée du séjour de chacun d'entre eux. Les résultats du traitement furent aussi inscrits tant à l'époque de leur congé qu'à celle de l'examen de rappel au milieu de 1959. Une étude statistique fut alors entreprise afin de déterminer s'il existait des différences valides entre les deux groupes. Les données furent soumises à l'épreuve de chi-carré. Au cours de la discussion les auteurs soulignent les problèmes que posent le diagnostic et le placement (qui dans plusieurs cas est inévitablement faux) de ces vieillards en quête de soins psychiatriques. Ils insistent aussi sur les difficultés inhérentes à la gestion d'une population gériatrique croissante dans les institutions pour aliénés.

NEVRALGIE DU TRIJUMEAU
ET HERPES SIMPLEX

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AUSSI LOIN qu'on remonte dans l'histoire de la médecine, on retrouve des citations sur la névralgie du trijumeau. Galien connaissait cette pathologie. Déjà au XI^e siècle, Avicenne la décrivait. Malgré son long passé et ses descriptions répétées, jamais on ne réussit à lui appliquer une étiologie satisfaisante. Le présent article n'a pas la prétention de mettre un point final à la recherche de la cause des névralgies du trijumeau, il ne veut que mettre en évidence une relation qui existe entre le tic douloureux et l'herpès simplex.

Du premier janvier 1956 au 31 décembre 1959, il y eut 80 hospitalisations à l'Hôtel-Dieu de Montréal pour tic douloureux du trijumeau. Ces 80 hospitalisations comprennent 72 patients, c'est donc dire que certains furent hospitalisés deux et même trois fois pour la même pathologie. De l'observation de ces patients, nous tenterons dans une première partie de relever les renseignements cliniques intéressants et dans une seconde nous discuterons la relation entre l'herpès et le tic douloureux du trijumeau.

ASPECT CLINIQUE

Fréquence

Sexe: Le sexe féminin semble plus touché que le sexe masculin. La proportion est d'environ deux

femmes pour un homme. Dans notre série de 72 patients, nous comptons 45 femmes et 27 hommes.

Age: La moyenne d'âge dans notre série était de 55 ans. Notre cas le plus jeune avait 17 ans et notre plus âgé, 80 ans. Une étude par décennie, nous montre une courbe qui répond bien à la courbe statistique de Lambert. Le maximum semble situé entre 50 et 70 ans. Trente-neuf de nos patients, soit 54%, avaient cet âge. C'est donc une maladie des dernières décennies.

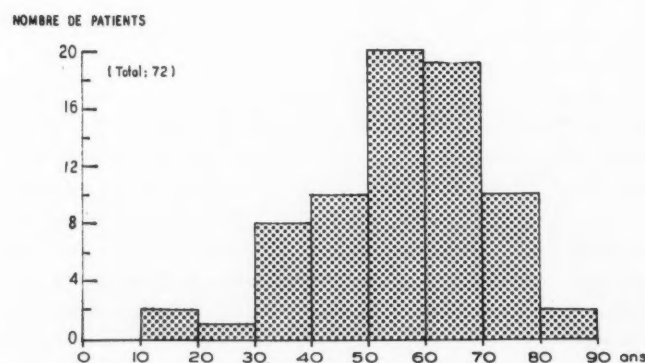


Fig. 1.—Fréquence selon l'âge.

Saison: La compilation de nos cas, nous a permis de trouver une fréquence saisonnière marquée de juin à septembre. Pour les quatre années, soit de 1956 à 1959, 47 patients furent traités pendant l'été, huit au printemps, 11 à l'automne et 14 à l'hiver. Il nous semble que ce décalage entre les saisons est beaucoup trop marqué pour n'être qu'un effet du hasard. Ainsi nous pensons que c'est surtout pendant l'été que les crises paroxystiques surviennent.

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NOMBRE DE CAS

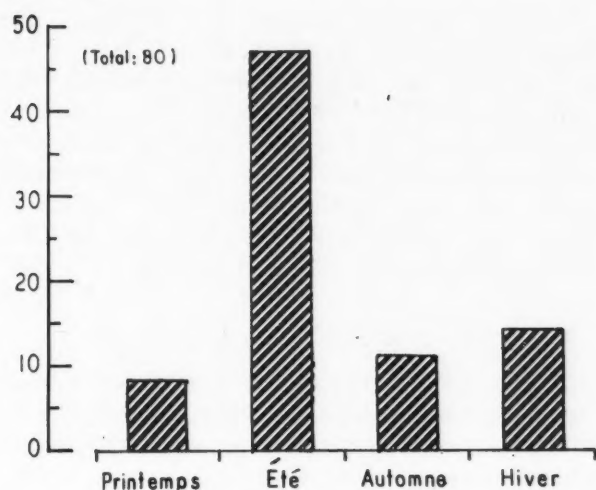


Fig. 2.—Fréquence par saison.

ETIOLOGIE

Les tics douloureux peuvent être classifiés en deux groupes: les tics douloureux essentiels et les tics douloureux secondaires. Dans le premier groupe, aucune étiologie satisfaisante n'a encore été prouvée. Dans le second, on retrouve toujours une cause irritative; soit mécanique, chimique, infectieuse¹ ou constitutionnelle. Les principales causes mécaniques consistent en une traction ou une compression de la racine sensitive du trijumeau par cicatrice, tumeur, anévrisme ou processus inflammatoire local. Les causes chimiques les plus fréquentes sont les intoxications à l'alcool et à l'arsenic. Les causes infectieuses reconnues sont la syphilis, la malaria, le typhus et le zona. Enfin les causes constitutionnelles les plus connues sont le rhumatisme, la goutte, le diabète, la syringo-bulbie et la sclérose en plaques.

Dans notre série de 72 patients, sept ont présenté un tic douloureux secondaire, soit 8.7%. Dans ce groupe, nous trouvons cinq cas de tumeurs: un méningiome gigantesque, un neurinome acoustique, une tumeur du ganglion de Gasser droit, un kyste épidermoïde de la fosse ponto-cérébelleuse droite et un kyste épidermoïde, du maxillaire supérieur gauche. Un cas était d'origine infectieuse soit un zona ophtalmique; cette observation est rapportée fréquemment dans la littérature.² Enfin notre dernier cas présentait de la sclérose en plaques. Ce patient d'ailleurs commença par accuser une névralgie à droite. Il subit une section de la racine sensitive du trijumeau à droite et fut soulagé définitivement de ce côté. Quelques mois plus tard cependant, il présentait un tic douloureux à gauche qui nécessita une seconde intervention.

Symptomatologie

On remarque d'abord que les patients les plus enclins à présenter de la névralgie du trijumeau sont des gens fatigués, émotifs, artérioscléreux et souffrant d'infections à répétition. La douleur en général est unilatérale: seul le cas de sclérose en

plaques a présenté une douleur bilatérale, mais encore cette bilatéralité n'était pas simultanée. Dans notre série, 44 patients présentaient une symptomatologie droite et 28, gauche. La localisation la plus fréquente était sur la deuxième et la troisième branche du trijumeau. Exceptionnellement était-elle trouvée sur la branche ophtalmique.

La crise paroxystique en général était provoquée par des mouvements volontaires comme parler ou mâcher et par des stimulations tactiles comme se frotter la lèvre. Les crises, chez nos patients, duraient de quelques secondes à quelques minutes. Quelques cas présentaient une douleur continue. La plupart des patients la décrivent ainsi: "J'ai l'impression que des milliers d'aiguilles me piquent en même temps." D'autres la décrivent comme un choc électrique qui parcourt la zone touchée. Dans la majorité des cas, les crises augmentent en nombre et en intensité avec le temps. C'est surtout l'été que les crises reviennent, puis il y a accalmie. Nous n'avons pas noté de régression définitive. Nous avons trouvé très peu de cas porteurs d'une zone déclenchante (trigger zone). Quand une telle zone existait, la plupart du temps, elle était située au repli naso-génien. Il ne faut donc pas attendre l'apparition de ce signe pour poser le diagnostic.

Pathologie

De fait, l'histopathologie donne peu de renseignements sur la névralgie du trijumeau. Les auteurs sont unanimes à dire qu'il n'y a pratiquement pas de changements morphologiques dans le nerf périphérique.¹ Certains auteurs rapportent des changements très peu caractéristiques dans le ganglion de Gasser: chromatolyse, rétraction du noyau, lésions fibreuses ou hypertrophiques.³ Ces variations sont vraiment trop inconstantes pour leur attribuer une signification particulière et il est difficile de dire si ces changements sont responsables des symptômes, puisque très fréquemment le ganglion est normal.

Traitement

Nous ne discuterons pas les différents traitements du tic douloureux du trijumeau, car une telle entreprise dépasserait le cadre de cet article. Contentons nous de décrire le mode de traitement de nos patients: 15 ont reçu un traitement essentiellement médical; 24 ont subi une alcoolisation; neuf une avulsion nerveuse et 32 une section des racines sensibles du trijumeau. L'évaluation de ces thérapies pourrait faire le sujet d'un autre article.

Relations entre tic douloureux du V et herpès simplex

C'est un fait connu en neurochirurgie qu'après une section des racines sensibles du V, un herpès simplex apparaît fréquemment.^{4, 5} Carton et Kilbourne prétendent même qu'il se produit dans 94% des cas.

Cushing, Richter,⁶ Aird,⁷ Carton et Kilbourne rapportent de nombreuses observations cliniques. Nous avons eu en 1959 l'occasion d'en observer plusieurs cas. En effet pour une raison inconnue, il y eut une augmentation marquée des hospitalisations pour tic douloureux: 38 patients furent hospitalisés. Ce chiffre est beaucoup plus élevé que celui des années précédentes: en 1956, 12 hospitalisations; en 1957, 14 et en 1958, 16. Cette augmentation nous a permis d'étudier davantage cette relation entre l'herpès et la névralgie du V. Nous avons aussi proposé quelques conclusions.



Fig. 3.—Malade opérée, montrant la localisation habituelle des vésicules d'herpès. A noter l'unilatéralité des lésions. Cette patiente avait subi une section de la racine sensitive du V à droite.

Dix-sept patients furent soumis à une section de la racine sensitive du trijumeau. L'opération consistait en une craniectomie sous-occipitale et après identification, section de la racine sensitive en protégeant les fibres ophtalmiques pour éviter les ulcérations cornéennes. Des 17 patients qui subirent une rhizotomie du V, pour tic douloureux essentiel, 13 présentèrent de l'herpès simplex, soit 76.5%. Cet herpès avait des caractères propres: apparition précoce de 48 à 72 heures après l'intervention, localisation unilatérale toujours du côté de la rhizotomie et sans jamais dépasser la ligne médiane de la face. Certains présentaient des lésions herpétiques sur la muqueuse de la joue. Dans tous les cas, l'herpès se situait sur le trajet de la deuxième et de la troisième division du V. Dans aucun, le territoire de la branche ophtalmique n'était atteint. Chez 18 patients traités par alcoolisation ou par avulsion nerveuse, un seul présenta de l'herpès. Ce patient au cours de la même hospitalisation avait d'ailleurs subi une alcoolisation du ganglion de Gasser et une avulsion du nerf sus-orbitaire.

Devant la constance de ce phénomène, la relation entre herpès et tic douloureux s'impose. Sa signification est moins évidente: la section serait-elle responsable de l'apparition d'un herpès latent par simple phénomène d'activation virale, ou alors, herpès et névralgie ne connaîtraient-ils pas une même étiologie? Certains caractères épidémiologiques et cliniques nous laissent croire à cette identité causale.

Traumatisme et activation virale

D'après Blank,⁸ Burnet et William, Scott, Steigman Convey, de 45 à 90% de la population portent une infection herpétique latente. Il ne suffit que d'un léger choc humoral pour provoquer une résurgence de l'activité virale et amener une manifestation clinique de l'herpès. La rhizotomie serait suffisante pour amener des changements locaux du métabolisme tissulaire et provoquer l'apparition de vésicules herpétiques.

Herpès et névralgie: étiologie identique

Quelques faits cependant échappent à l'explication de la suite des phénomènes décrits plus haut. Pourquoi dans nos cas l'herpès est-il unilatéral? Il est prouvé qu'il s'agit bien d'herpès simplex et non de zona. Carton et Kilbourne l'ont démontré par des identifications virologiques. La manifestation clinique commune de l'herpès récidivant est en général bilatérale. Cette affirmation est étayée par des faits expérimentaux: l'élévation thermique provoquée entraîne chez certains patients l'apparition d'herpès, mais cet herpès est symétrique et bilatéral.⁹

A part ces réserves, certains arguments plaident en faveur d'une étiologie commune.

1) Terrain. Il existe une analogie remarquable entre les deux pathologies. C'est le même genre de malades qui en sont frappés: les nerveux, les émotifs, sujets aux infections répétées. L'évolution clinique est la même: périodes d'exacerbation suivies de périodes d'accalmie. Entre les crises, les sujets se sentent parfaitement bien.

2) Fréquence saisonnière. La fréquence des crises névralgiques semble culminer dans la saison chaude, période à laquelle éclatent également les infections virales. L'année 1959 nous en fournit un exemple frappant: à Montréal, pendant la saison estivale, deux épidémies virales semaient la consternation; une épidémie de poliomyélite touchait près de mille personnes et une épidémie à Cocksackie en forçait plusieurs centaines à s'aliter. Simultanément, on nota une telle augmentation du nombre d'hospitalisations pour tic douloureux, que c'en était presque une épidémie.

3) Conditions de l'apparition de l'herpès. Nous avons parlé plus haut d'une activation virale par traumatisme chirurgical. Ce traumatisme seul est-il vraiment une condition suffisante? Il semble que non. En effet, l'exérèse de certaines tumeurs cérébrales nécessite parfois l'exploration du ganglion de Gasser et même occasionnellement la section de la racine sensitive du V sans pour autant déclencher l'apparition d'herpès simplex. En plus du traumatisme chirurgical, il faut donc une condition clinique préalable bien définie pour l'existence d'un tic douloureux. Puisque l'herpès post-opératoire est non seulement unilatéral mais aussi ipsilatéral, n'est-on pas en droit de supposer que le ganglion ou les trois branches du V recéleraient ce même virus? Pour une raison inconnue, le

traumastisme chirurgical favoriserait l'efflorescence cutanée. Il est bien évident que pour prouver définitivement l'étiologie virale du tic douloureux il faudrait identifier le virus, soit dans le ganglion, soit dans le nerf périphérique. Plusieurs auteurs croient que le virus de l'herpès entre les épisodes cliniques, logerait dans le ganglion de Gasser et le nerf périphérique. Goodpasture,¹⁰ Gastinel,¹¹ Howard, Freeman semblent de cet avis. Jamais cependant on n'a pu démontrer la présence de virus dans ces ganglions. Carton et Kilbourne n'ont pas réussi à isoler de virus herpétique des ganglions de Gasser de deux patients opérés pour tic douloureux et pourtant ces deux malades ont chacun fait des vésicules d'herpès dans les suites opératoires. Il faudrait donc une étude plus poussée de ces ganglions avec, en plus de recherches virologiques, des colorations histologiques spécifiques qui pourraient nous révéler la présence ou au moins des signes du passage du virus dans le ganglion. De telles techniques sont décrites par Blank.⁸

CONCLUSION

Le présent article ne prétend pas élucider complètement le problème de l'étiologie du tic douloureux du trijumeau. Il ne fait que mettre en lumière la relation qui existe entre le tic douloureux et l'herpès simplex. Il propose une hypothèse de travail que l'avenir se chargera de confirmer ou d'infirmer. Ces quelques faits soulignent l'importance de reprendre l'étude de l'étiologie pour voir s'il y a relation de cause à effet. Nous tentons actuellement d'établir cette relation en nous servant des critères cités plus haut.

RÉSUMÉ

Nous présentons 80 cas de tic douloureux du V hospitalisés à l'Hôtel-Dieu de Montréal de 1956 à 1959. Une étude clinique donne les renseignements suivants: âge moyen: 55 ans avec une fréquence marquée surtout entre 50 et 70 ans; les femmes en sont deux fois plus souvent affectées que les hommes;

au point de vue de la distribution saisonnière, les crises sont plus fréquentes en été que pendant les autres saisons.

Dans un groupe de 72 patients, sept ont présenté des tics douloureux secondaires et 65 des névralgies essentielles. Les symptômes se sont manifestés 44 fois du côté droit de la figure et 28 fois à gauche.

La discussion met en évidence la relation entre herpès et tic douloureux. Deux hypothèses sont proposées. La première veut que la section de la racine sensitive active un herpès latent. La seconde prétend que la névralgie du trijumeau et l'herpès simplex ont une étiologie virale commune.

Enfin les auteurs proposent une hypothèse de travail qui pourrait définir d'une façon quasi certaine l'étiologie virale de la pathologie.

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SUMMARY

The present study deals with 80 patients suffering from tic douloureux of the trigeminal nerve, hospitalized at Hôtel-Dieu of Montreal between 1956 and 1959. The average age of the patients was 55, the greatest number being between 50 and 70 years of age. The sex incidence was two females to one male. The painful bouts were more frequent in summer than in any other season.

Out of 72 patients, seven had tic secondary to another pathological condition while 65 appeared to be idiopathic. Symptoms were more frequent on the right than on the left side (44 on the right and 28 on the left).

The discussion emphasizes the relation between herpes and tic douloureux. Two hypotheses are considered. The first one suggests that a latent herpes is activated by section of the sensory root. The second hypothesis is that both trigeminal neuralgia and herpes simplex have a common viral etiology.

Finally, the authors present a working hypothesis for definite verification of the viral etiology of the lesion.

THE MOVE TO SIMPLIFY LIFE

The nineteenth century saw a great movement toward sanitation. May not the twentieth century, before it is through, see a great movement toward simplification of life, toward a restoration of conditions that seem at the same time closer to real happiness and to real health? The relation between the two remains largely in the field of the unknown, but that they are related one feels in one's bones. And so while Americans congratulate themselves on what they have achieved to improve the health of the people, to find cures and to develop treatments, they should not forget—doctors and laymen alike—the great work of social reformation that underlies medicine as it underlies politics. Science is at the heart of the problem, but beyond science there are the qualities of humane living and of a sane environment that scientists and philosophers have sought together since the rise of civilization. The quest continues. All are summoned to do their part.—A. Heckscher: *New England J. Med.*, 262: 23, 1960.

THE ROOTS OF MENTAL HEALTH

Among the most significant developments in psychiatry during the past quarter of a century has been the steady growth of evidence that the quality of the parental care which a child receives in his earliest years is of vital importance for his future mental health.

The infant and young child should experience a warm, intimate and continuous relationship with his mother (or permanent mother-substitute) in which both find satisfaction and enjoyment. It is this relationship with the mother, varied in countless ways by relations with the father and siblings, that child psychiatrists and many others believe underlies the development of character and mental health.

It follows that broken homes are likely to produce behaviour disorders in children, and this has been confirmed by several studies.—*Mental Illness and Mental Health in the World Today*. WHO Pan American Sanitary Bureau.

CLINICAL EXPERIENCE WITH TRIFLUOPERAZINE IN LOW-GRADE MENTAL DEFECTIVES

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THE CARE of mentally defective patients, especially in the lower grades of deficiency, frequently involves dealing with patterns of behaviour which are similar to, but not identical with, those of disturbed psychotics. Aggressiveness, destructiveness, self-abuse, noisiness, and overactivity occur commonly, and, until the advent of the tranquillizing drugs, could be controlled only indifferently by sedatives or physical restraint.

At the Manitoba School, each of the new tranquillizers has been tried as it became available, beginning with reserpine, and all have proved valuable, to a greater or lesser extent, in controlling undesirable symptoms of low-grade defect and in eliminating the necessity for physical restraint or the administration of heavy doses of sedatives.

In assessing the problem of overactivity in its various forms, it has been possible to differentiate the chronic from the episodic or phasic type, and these differing symptomatology have been found to be amenable to different therapeutic approaches. Unstable aments whose overactivity has been of a chronic and persistent nature have responded to treatment with orally administered tranquillizers, while those showing unpredictable, episodic, or phasic disturbances have usually been successfully controlled by the use of injectable forms.

Investigation of the effects of trifluoperazine dihydrochloride, a phenothiazine derivative, on the behaviour of mentally defective patients has been reported by Rudy *et al.*,¹ by Rettig, Caldwell and Josephs,² by Lawlis,³ and by LeVann.⁴ All found the drug to be effective in many cases where nursing care is complicated by disturbed behaviour of the types referred to above. The purpose of the present paper is to give the results of fairly widespread use of the drug in low-grade defectives whose behaviour-pattern is unstable.

Over the course of the past 18 months, extensive use has been made of trifluoperazine, using tablets, fluid concentrate and injectable forms. The drug was formally evaluated in 57 disturbed low-grade patients who evinced one or more of the target symptoms mentioned above. Of the total of 57 patients, 17 were considered to be episodically disturbed, while the remaining 40 were of the chronic type.

DESCRIPTION OF PATIENTS

Thirty female and 27 male patients were studied. Ages ranged from eight to 49 years among the females, and six to 62 years among the males.

TABLE I.—DIAGNOSIS—GRADE OF DEFECT

	Idiots	Imbeciles	Morons	Totals
Males.....	15	10	2	27
Females.....	13	16	1	30
Totals.....	28	26	3	57

Grades of defect for both males and females are shown in Table I. Three morons had organic complications which accounted for their disturbed behaviour—epileptic deterioration in one case, and epilepsy with psychosis in the other two.

DIAGNOSIS

Fifteen cases were of the familial type without stigmata, while 18 cases were of the heavily stigmatized type sometimes referred to as oligoencephalic. The remaining cases included eight other conditions.

TABLE II.—DIAGNOSIS—ETIOLOGY

	Familial without stigmata	Familial with stigmata	Cerebral palsy	Diffuse brain injury	Mongo- lians	Epileptic amentia
Males	5	10	4	2	1	3
Females	10	8	4	3	1	2
Totals	15	18	8	5	2	5
	Oxy- cephaly	Retrolental fibroplasia	Severe infantile autism	Congenital word deafness	Totals	
Males	—	1	1	—	27	
Females	1	—	—	1	30	
Totals	1	1	1	1	57	

TARGET SYMPTOMS

All patients in the group showed one or more of the following symptoms: destructiveness, self-abuse, noisiness, abusiveness (physical) towards other patients or staff members, and motor overactivity. In a test period of two weeks before the drug was commenced, all medications (except anticonvulsants) were discontinued, while the ward situation was observed to establish a general behaviour-level for each patient.

DOSE RANGE AND METHODS OF ADMINISTRATION

In all adult patients who were given the drug orally, doses of 5 mg. thrice daily were administered initially. Some control of target symptoms usually became apparent within a week, such effect being often observed from one to four days after the first day of treatment. If no control was achieved in 10 days, the dose was doubled. In the face of continuing absence of response, the dose was raised to 20 mg. thrice daily. As soon as control of symptoms was achieved, the t.i.d. dosage was reduced to b.i.d. administration and maintained at that level unless the onset of side effects occasioned a further reduction in dosage. It was found that patients who did not respond to 20 mg. thrice daily developed such a degree of drowsiness that the drug had to be discontinued. Smaller or younger patients were

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started on 1 or 2 mg. thrice daily, the dose being increased until control was achieved, then reduced to b.i.d. administration as in the case of the adults.

Patients whose disturbed behaviour was of an episodic or phasic type were placed on a p.r.n. (an "as required") injection of 2 mg., rising to 4 and then 6 mg. depending on response. Once the optimum dose was established, such cases usually responded to a single daily injection, although a few repeat doses were given in the early part of the series, before optimum dosage had been established for each patient.

RESULTS

Of the 40 patients taking the oral form of trifluoperazine, four showed *no* response, or else developed such a degree of drowsiness that the drug had to be withdrawn. Nine patients showed a *fair* response, as evidenced by some diminution in frequency and/or severity of target symptoms. In 14 patients a *good* response was obtained, as evidenced by marked diminution in frequency and/or severity of target symptoms, and in 13 patients an *excellent* response, as evidenced by complete control of one or more target symptoms and marked diminution in frequency and/or severity of the remainder.

TABLE IIIA.—RESULTS—ORAL ADMINISTRATION

	<i>Excellent</i>	<i>Good</i>	<i>Fair</i>	<i>Unimproved</i>	<i>Totals</i>
Males	7	9	6	2	24
Females	6	5	3	2	16
Totals	13	14	9	4	40

Of the 17 patients treated with the injectable form of the drug, two were unimproved, three had a fair response, five a good response, and seven an excellent response in terms of degree of control of episodic target symptoms achieved by a single injection.

TABLE IIIB.—RESULTS—PARENTERAL ADMINISTRATION*

	<i>Excellent</i>	<i>Good</i>	<i>Fair</i>	<i>Unimproved</i>	<i>Totals</i>
Males	1	1	1	0	3
Females	6	4	2	2	14
Totals	7	5	3	2	17

The effect of successful treatment of a number of low-grade defectives in any ward is a marked improvement in the general ward environment, and this, by diminishing the incidence of noisy and disturbing stimuli upon unstable patients, is reflected by a further improvement in behaviour.

SIDE EFFECTS

Eighteen (45%) of the 40 patients treated with oral trifluoperazine developed side effects. Of these, five exhibited symptoms of extrapyramidal tract involvement, nine developed dystonic symptoms, two

became transiently overactive, and two developed a marked degree of drowsiness. (The latter two patients were receiving a high dosage of the drug, and failed to respond therapeutically.) The extrapyramidal and dystonic side effects were encountered at widely variable times in the treatment period, some occurring during the first few days, some from one to two weeks, and some from four to six weeks after the commencement of treatment. As soon as these side effects were recognized, trifluoperazine was omitted for from 12 to 48 hours, and the patient was started on procyclidine in doses of 15 to 30 mg. daily. Trifluoperazine was resumed at half the dose, being given when the side effects appeared, as soon as the

TABLE IV.—SIDE EFFECTS—ORAL ADMINISTRATION

	<i>Extra-pyramidal symptoms</i>	<i>Dystonia</i>	<i>Drowsiness</i>	<i>Over-activity</i>	<i>Totals</i>	<i>Total treated</i>
Males	3	6	1	1	11	24
Females	2	3	1	1	7	16
Totals	5	9	2	2	18	40

patient was clinically free of frank parkinsonism or dystonia. It was usually found possible to return to the optimum maintenance dosage level gradually without occasioning a return of side effects. A smaller incidence of side effects would probably have resulted from a dosage regimen involving a small initial dose and a slow increase in dose until control was achieved. This method of administration has now been adopted generally to control disturbed behaviour in low-grade patients. Two patients, however, because of a previously sullen, moody, and negativistic disposition, were continued on trifluoperazine in doses of 10 mg. twice daily for several days after the onset of parkinsonian rigidity and mask-like facies. As a result, their side effects persisted for three weeks after withdrawal of the drug, during which time they were receiving 30 mg. of procyclidine daily.

Apart from the side effects mentioned above, no evidence of urinary abnormalities, blood dyscrasias, hypotension, skin rashes, or jaundice was found in any of the patients in the series.

Two of the 17 patients treated with injectable trifluoperazine had side effects of the dystonic type. In both cases, side effects occurred five to six hours after administration of the drug, persisting for two hours in one case and for four hours in the other. One case responded satisfactorily to reduction of dosage from 6 mg. to 4 mg., although there was a less effective control of overactivity at this dosage level than in the remaining patients at their optimum dose. In the other case, side effects recurred with all but the smallest doses, and the drug was withdrawn. This patient also reacted violently to the oral form of the drug, even in small doses. In the remaining 15 patients there were no side effects. In view of the relatively late onset of

side effects (five or six hours after injection), repeated daily doses of trifluoperazine were abandoned early in the series, and improved control was sought by adjustment of single dosage alone.

CONCLUSIONS

Trifluoperazine appears to be a drug of choice for the control of destructive, self-abusive, noisy, abusive, and overactive behaviour in low-grade mental defectives. The oral form of the drug, administered in twice-daily maintenance doses, controls a high proportion of chronic symptoms of this type, while single injections can frequently be used to control the same symptoms when they occur episodically or phasically. Side effects are fairly common, but can be readily controlled by omitting the drug for 12 to 48 hours, with the concurrent administration of an anti-parkinsonian drug such as procyclidine in full adult dosage. By the methodical use of this drug, the use of physical restraint measures can be virtually abolished in an institutional setting. Trifluoperazine is effective over a wide range of conditions associated with mental deficiency, and is as effective in patients with cerebral palsy and diffuse brain injury as it is in stigmatized and unstigmatized familial defectives.

SUMMARY

Trifluoperazine has been utilized effectively in controlling overactivity, abusiveness, self-abuse, noisiness, and destructiveness in 30 female and 27 male low-grade mental defectives. Methods of achieving optimum dosage have been described. The incidence of side effects and methods of dealing with them are

reported. The use of the oral form in chronically disturbed patients, and of the injectable form, on an "as required" (p.r.n.) basis, in episodically or phasically disturbed patients is recommended.

I am indebted to Dr. H. S. Atkinson, Medical Superintendent, The Manitoba School, for permission to use the clinical material presented in this paper.

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RÉSUMÉ

On a cherché à contrôler la suractivité, l'agressivité, l'onanisme, le tapage et les tendances destructives d'une collection de 57 idiots, imbeciles et débiles des deux sexes et d'âges divers. Après une période témoin de deux semaines au cours de laquelle toute médication (sauf les anticonvulsants) fut supprimée, on administra 5 mg. de trifluopérazine trois fois par jour *per os* aux adultes et 1 ou 2 mg. aux enfants. En absence d'amélioration, la dose fut augmentée au bout de 10 jours. On administra le médicament par injection chez 17 d'entre eux. Quatre des 40 malades traités oralement n'ont montré aucun effet ou alors devinrent si somnolents qu'on dut cesser le traitement; on obtint des résultats assez bons chez neuf malades de ce groupe, de bons résultats chez 14 et des résultats excellents chez 13. Les effets furent comparables chez ceux qui reçurent le médicament par injection. Des effets secondaires furent observés dans 45% des cas sous forme de manifestations extrapyramidales ou dystoniques qui disparurent avec la diminution de la dose ou l'administration d'antiparkinsoniens. L'auteur conclut que l'emploi, de trifluopérazine facilite considérablement la direction d'une salle d'agités et produit des effets même dans des cas de déficience mentale.

AXILLARY ARM BLOCK WITH EMPHASIS ON ITS USE IN CHILDREN*

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THERE IS an awakening interest in the technique of anaesthetizing the brachial plexus at the lower margin of the axilla. This technique has been variously called upper arm block, axillary block or brachial block by the axillary route. This last term is confusing because the plexus may be blocked above the first rib by a long needle introduced through the axilla.

Axillary block was described by Accardo and Adriani¹ in 1949. Adriani mentioned the necessity for paræsthesia for successful block—in the little

finger for ulnar nerve block; on the back of the hand for radial nerve block; at the elbow for musculocutaneous nerve block, and at the tip of the fingers for median nerve block. Although some anaesthetists have used this block for many years, it is likely that Clayton and Turner² can be thanked for the revival of interest in this technique.

Burnham reports his introduction to this block in *Current Comments in Anaesthesiology*. It is a happy coincidence that the preceding comment was concerned with an article by Betcher on hypno-induction techniques in paediatric anaesthesia. These hypnotic techniques contribute to the success and delight in using the axillary block technique in children.^{3, 4}

TECHNIQUE

This has been excellently described and illustrated in drawings by Clayton and Turner,² Hudon and Jacques⁵ and Burnham.³

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Briefly, the technique used in our cases is the following. The axilla has been shaved where necessary and a proper surgical preparation has been done. With the patient in the supine position, the arm is abducted 95° from the side and in a neutral position of supination and pronation. The axillary artery is palpated $\frac{3}{4}$ inch above the lower margin of the axilla, where it lies along the lateral wall. The coracobrachialis and the pectoralis muscles lie anteriorly to it. Sometimes when palpation is done posteriorly, the profunda artery can be palpated; failure will result if this is used for the landmark.

All blocks have been done with a $\frac{3}{4}$ -inch, 25-gauge needle. For adults, 2% lidocaine (Xylocaine) has been used, 6-10 c.c. being deposited at each of four places (see below). No adrenaline was used because it was found that even as little as 1/200,000 caused sufficient spasm of the axillary artery to make palpation difficult. In children, 1-1½% lidocaine has been used and the amount deposited was 3-7 c.c. in the four sites, making sure that the total dose was below the toxic dose for that age.

Injections are made at four places: (1) A wheal is raised in the skin over the axillary artery and the underlying tissue is infiltrated. This will anesthetize the intercosto-brachial nerve, the medial cutaneous nerve of the forearm, and the medial cutaneous nerve of the arm. (2) Injection is made above the artery to anesthetize the median nerve. The needle is kept close to the artery. A definite "give" is felt as the needle penetrates the fascia covering the nerves and vessels. The musculocutaneous nerve has some variety in its relation here, and, where it separates from the plexus slightly higher, may already lie in the substance of the coracobrachialis muscle at this level. Injection made above the artery should be distributed superficially and continued down to a depth just short of the humerus. If the musculocutaneous nerve is missed, there will be no anesthesia along the posterolateral part of the forearm. (3) The needle is passed under the artery (posteriorly) to block the ulnar nerve. (4) The arm is then supinated and injection is made below and behind the axillary artery to block the radial nerve.

Aspiration is done carefully and frequently, both before and during injection. If blood is aspirated, the needle is withdrawn and pressure put over the area for a couple of minutes. The needle is re-introduced close to the area and the technique continued. Paræsthesiæ were not purposely elicited although they frequently occurred. Needles are examined before use as the whole length of the needle is used and the possibility of breakage must be considered.

Anesthesia takes 20 minutes to become complete. More anesthetic agent can be added at this time if there is any defect in the block. In the event of failure to anesthetize one nerve, it may be blocked at a more peripheral site.

Sedation has both advantages and disadvantages. In some cases, it helps management of the patient and prepares the way for a general anesthetic, if such becomes necessary. On the other hand, the axilla is not a tender area and once the initial wheal is made there is no further discomfort. Sedation prolongs the hospital stay because one must both wait for the sedation to become effective and keep the patient longer after the surgery is completed. The "drying" effect of belladonna drugs is so disturbing in children that it becomes most difficult to use suggestion as part of this technique.

LIGHT HYPNOSIS

One of the first youngsters was quite amused by his ability to contract his muscles, and, much to the consternation of the surgeon, kept displacing his fracture. He was asked to turn his head to the side, close his eyes, breathe quietly and fairly deeply through his mouth and let himself go off to sleep. Much to our surprise, this active seven-year-old was asleep in a few moments.

About 70% of the children can be put to sleep easily by this method. They are ideal candidates for suggestion. Most of them have a full stomach and have been fatigued by fear, crying and pain. Now with reassurance, loss of pain and perhaps some help from the lidocaine, they are asleep so soon that the nursing staff looks on in awe.

DISCUSSION

This technique has been used for surgery in the upper limb, below the elbow, for age groups extending from 16 months to 80 years. Over 100 such blocks have been performed with failure rate of 5% at present. Occasionally there has been evidence of bone or periosteal pain at the moment the fracture is reduced. For adults we have used 50% N₂O/O₂ until they are drowsy. Children, asleep from suggestion, may wince but many do not wake up. Some patients required a small amount of sodium thiopental (Pentothal) and/or pentobarbital for restlessness.

Often the block is done as soon as the child reaches the hospital. This makes the work of the x-ray department much easier. The children can be in and out of hospital within an hour.

Analgesia is sleeve-like up to the point of block. Tourniquets have been used with no further block. Patients were aware of the inflation of the tourniquet but there was no pain. The duration of the block has been extended to three to four hours with the help of adrenaline.

Children with injuries, especially fractures, must be considered to have a full stomach in most cases. It is this danger that makes such a technique of prime importance in the out-patient department.

The block has not been performed in the face of an infection of the upper arm.

SUMMARY

Neurological block of the brachial plexus in the axilla has been described. This method of anaesthesia is of particular value in children where it may be combined with a light hypnotic state. Such a technique can be of great value in the out-patient department. It overcomes the danger of a full stomach, shortens hospital stay and has no serious complications. The block can be performed readily and should have a high success rate for the occasional user. It allows the use of a tourniquet. Since pneumothorax is not a problem, this block may be used bilaterally.

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RÉSUMÉ

Les auteurs commentent une technique d'anesthésie des nerfs du bras dans la région axillaire qu'ils ont employée chez plus de cent malades. Ce procédé est très utile chez les petits enfants surtout si on y ajoute comme dans la présente série un léger état d'hypnose. Il permet l'application d'un garrot et se prête à la plupart des interventions chirurgicales au-delà du coude. L'anesthésie fut obtenue par injection périartérielle d'une solution de 1 ou 2% de lidocaïne dans le voisinage de l'artère axillaire à la marge inférieure de cette région. On pratiqua l'injection à l'aide d'une aiguille No. 25 de 2 cm. de long. La plupart des 5% d'échecs se comptèrent chez les adultes. Il n'y eut aucune complication sauf une légère sensibilité à l'endroit de l'injection. Cette technique permet d'éviter les risques que présente chez les enfants l'anesthésie d'un sujet qui n'est pas à jeun.

Case Reports

SUBDURAL HÆMATOMA
COMPLICATING ANTICOAGULANT
THERAPY

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THE HAZARDS of hæmorrhage from the use of anti-coagulants have been well documented. Their use in the prevention of a thromboembolic phenomenon is recognized, but the possibility of hæmorrhage is a calculated risk. This possibility must always be weighed against the benefits.¹

This report concerns subdural hæmatoma complicating anticoagulant therapy, a rare but serious complication. Report of a case with bilateral involvement and subsequent recovery after surgery is given, and the literature is reviewed.

A.F., a 75-year-old Jewish man, was admitted by ambulance to St. Boniface Hospital in the afternoon of November 7, 1955. He was confused and stuporous, but responded to painful stimuli. His previous history revealed that he had an acute posterior myocardial infarction on July 22, 1955, and was placed on long-term anticoagulant therapy in the form of bishydroxycoumarin (Dicoumarol).

His present illness began on November 1, 1955, with severe frontal headache, unrelieved by analgesics. Two days later he developed urinary incontinence and mental confusion. He also began to vomit. On admis-

sion, the following pertinent physical findings were noted. The left pupil was fixed and enlarged; the pulse rate was 62 per minute; the blood pressure (B.P.) was 150/80 mm. Hg, and a positive plantar response (Babinski) was present on the left side. There was no history of head injury or of previous cerebrovascular accident.

The prothrombin time was 47 seconds (10%). Skull films showed the calcified pineal body to be midline in position, but lower and more posterior than usual. His chest radiograph was reported as normal.

In the early morning of November 8, 1955, he responded poorly, although he was conscious. The nurse noted bloody urine and he had vomited dark red fluid. By noon, respirations were of Cheyne-Stokes type. At 2.30 p.m. the same day, ventriculography was done; air was introduced through a twist drill hole in the right parietal bone. Films revealed a marked shift from left to right of the right lateral ventricle and the third ventricle, with marked depression particularly in the anterior portion. The basilar cisterns were markedly compressed. No air was present in the left lateral ventricle. The findings were reported as non-specific, but suggested a large space-occupying lesion, possibly a subdural hæmatoma, on the left side. The ventricular fluid was clear and colourless, with a protein value of 18 mg. %. Microscopically, many red blood cells were noted in this fluid.

Bilateral burr holes were performed shortly after. A large subdural hæmatoma was found on the left side. There was also a subdural hæmatoma on the right side, containing three separate membranes. The hæmatomas were evacuated. The patient was conscious postoperatively. His pupils were equal and both plantars were flexor in response. He received 50 mg. of vitamin K₁ (Mephyton) intravenously, and the prothrombin time was 14.5 seconds (70%) the following day.

The headache continued but was less severe. After further intravenous vitamin K₁, his prothrombin time was 14.2 seconds (90%) on November 11. On the next day, he was up walking for short periods.

On November 13, he felt less steady on his feet and his speech was noticeably less clear. He became

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TABLE I.—SUMMARY OF CASES OF SUBDURAL HÆMATOMA COMPLICATING ANTICOAGULANT THERAPY REPORTED IN THE LITERATURE

Author	Age	Sex	Indication for anticoagulation	Associated conditions	Complications	Lowest prothrombin time	Days after onset of anticoagulation	Outcome	Autopsy findings
Shlevin and Lederer ²⁷	79	F	Right retinal vein thrombosis	Long-standing hypertension; chronic anaemia	Hæmaturia; bleeding gums; ecchymoses; heart failure; atrial fibrillation and coma	360+ sec. (normal control not given)	28	Death	Bilateral subdural hæmatomas; clotted blood in base of skull; hæmorrhages in subarachnoid space, retroperitoneal tissues, renal pelvis, urinary bladder, stomach and duodenum
Nathanson <i>et al.</i> ²⁸	69	M	Embolization	Hypertension; auricular fibrillation	Occipital headache; fixed pupils; coma; xanthochromic CSF, later bloody; ankle clonus; absent corneal reflexes; hyper-reflexia	21 sec. (normal control not given)	6	Death	Subdural clot over left parietal lobe; hæmorrhage in corpus callosum, tegmentum, base of pons and lower midbrain
"	64	M	Previous coronary occlusion followed by atrial fibrillation. Recurrence of substernal pain	—	Frontal headache; irritable, confused, disorientated; left facial weakness; pineal body shifted to the left; diagnosis of right subdural hæmatoma made	54 sec. (normal control not given)	30	Bilateral burr holes revealed bilateral subdural hæmatomas. Patient recovered	—
"	65	F	Phlebitis of legs	—	Headache; lethargy; confusion; disorientated; neck rigidity; microscopic hæmaturia; blood-tinged CSF; bilateral subdural hæmatomas diagnosed on basis of right carotid angiogram	71 sec. (normal control 12 sec.)	48	Surgery twice. Patient died	Site of bilateral subdural hæmatomas confirmed; no residual clot
Eisenberg ²⁹	56	M	Myocardial infarction twice	Mild diabetes mellitus and mild congestive heart failure	Dilated, fixed right pupil; left side of face and body flaccid; bilateral Babinski response; coma	8% (normal control not given)	70	Patient died postoperatively	Right subdural hæmatoma over temporal lobe
Barron ²³	60	F	Pulmonary embolization	Hypertension; cardiomegaly; obesity	Headache; coma; right pupil dilated; right limbs flaccid; CSF bloody	38.2 sec. (normal control 12 sec.)	23	Death	Subdural hæmatoma over right frontal and parietal lobes; hæmorrhage in tegmentum of pons and midbrain; caudally ruptured into 4th ventricle; blood in subarachnoid space over right frontal lobe

Dicoumarol was the anticoagulant involved in the above cases.

drowsy, and his left pupil was seen to be larger. A positive plantar sign (Babinski) was again present on the left side.

The prothrombin time on the following day was 13.8 seconds (100%). From then on there was progressive improvement, and he was discharged on December 9, 1955, in good condition.

This patient did well until August 5, 1958, when he suffered another myocardial infarction. On August 12, 1958, he had a recurrence of severe chest pain and died the next morning from intractable congestive heart failure. Permission for post-mortem examination was not obtained.

DISCUSSION

Contraindications to the use of anti-coagulants are many. The most important ones are lack of adequate laboratory facilities and trained technicians, lack of experience and competence on the part of the physician, and lack of patient co-operation and intelligence.²

Certain contraindications have been listed by different authors.^{2, 8}

A. Medical: (1) Purpuras of any kind. (2) Blood dyscrasias and bleeding tendencies. (3) Severe hypertension, particularly with a history of previous cerebrovascular accidents. (4) Active or imminent ulcerative or bleeding lesions of the gastro-intestinal or genito-urinary tract. (5) Subacute bacterial endocarditis.

B. Surgical: (1) Brain and spinal cord surgery. (2) Large, open, raw surfaces with poorly controlled hæmostasis. (3) Deep needle-puncture procedures, e.g. lumbar sympathetic blocks.

C. Obstetrical and gynæcological: (1) Recent threatened abortion. (2) Incomplete abortion. (3) Pregnancy near term.

Cautious use is advised in patients with chronic congestive heart failure, hepatic insufficiency, and renal disease, and in nutritional deficiencies.^{2, 3, 8-11}

Factors that may modify the stability of prothrombin time include infections, diarrhoea, shock, menstruation, excessive alcoholic consumption, vitamin C deficiency, and administration of large amounts of salicylates, sulfonamides, and bowel-sterilizing antibiotics.²

Jaques¹² claims that stress through its effect on blood vessels is one of the commonest exciting causes of hæmorrhage. Differences in individual susceptibility, as suggested by Prandoni and Wright,¹³ may be responsible in part for hæmorrhagic responses.

Other complications besides bleeding are agranulocytosis,¹⁴ purpuric forma-

tion,¹⁵ hypersensitivity reaction, hepatitis, jaundice and leukæmoid reaction.^{16, 17} Side reactions such as diarrhœa, dryness of mouth, polydipsia, polyuria and tachycardia may occur.²

Hæmorrhage accompanying anticoagulant therapy may present as microscopic or gross hæmaturia, epistaxis, gingival bleeding, conjunctival hæmorrhage, cutaneous ecchymosis, hæmatoma, hæmoptysis, hæmarthrosis, periosteal hæmorrhage, and bleeding into the pericardial sac, pleural cavity, uterine cavity, gastro-intestinal tract and retroperitoneal tissue.^{2, 7, 18-23}

Hæmorrhage may occur in the central nervous system during anticoagulant therapy, particularly in hypertensives with previous cerebrovascular accidents.²³ These may be intracerebral,^{3, 7, 23-25} intracerebellar,²³ intraventricular,^{23, 26} subarachnoid,^{7, 23, 27} subdural,^{23, 27-29} or intraspinal³⁰ or extradural hæmorrhage of the spinal cord,³¹ or hæmorrhage in the mid-brain, pons or medulla oblongata.^{23, 28}

Six cases of subdural hæmatoma complicating anticoagulant therapy have been found in the literature. Three of the cases had bilateral subdural hæmatomas, and only one patient survived. Table I is a summary of these cases.

In each of these patients the prothrombin time was prolonged beyond the safety margin. This emphasizes the importance of careful supervision of patients during anticoagulant therapy and the necessity of frequent readjustment of dosage according to accurate prothrombin-time determinations.

Three of the patients had evidence of hypertension. In Barron's²³ review of the literature on intracranial hæmorrhage from anticoagulants, he pointed out that six of the 58 cases were of hypertensives. These were associated with fatal intracerebral hæmorrhage. Of the six patients he reported, two were hypertensive, and one was receiving anticoagulant therapy at the time of fatal hæmorrhage.

Apparently none of the patients gave any history of head injury, nor was there any clinical evidence of such. No doubt the possibility of minor or trivial trauma to the head directly or indirectly, which might have initiated bleeding intracranially, cannot be entirely excluded. Of course, with evidence of head injury in patients receiving anticoagulants, added suspicion of subdural hæmatoma must be raised in view of the seriousness of this complication and the high mortality rate. Three of the six cases reported in the literature had bilateral involvement of the subdural space. Only one patient survived. As far as we know, our case is the second one that was treated successfully for bilateral subdural hæmatomas complicating anticoagulant therapy.

In all the cases with subdural involvement, the anticoagulant concerned was bishydroxycoumarin.

With more widespread use of other anticoagulants, this complication will eventually follow their use also.

The incidence of hæmorrhages in patients on anticoagulant therapy ranges between 5.7 and 42%, reported by different investigators.^{20, 24, 32} Most of these are minor hæmorrhages. Major hæmorrhagic complications are rare.^{2, 10} They are usually not dangerous, and can be easily controlled by vitamin K.^{2, 9} Nevertheless, one must bear in mind the possibility of fatal results.

SUMMARY

A case of bilateral subdural hæmatomas in association with bishydroxycoumarin therapy, with subsequent recovery, is reported.

A review of the literature concerning contraindications to the use of anticoagulants and the hæmorrhagic complications resulting from anticoagulant therapy is presented, with emphasis on central nervous system involvement.

The possibility of fatal hæmorrhage accompanying anticoagulant therapy must be kept in mind.

The correct diagnosis in this case was first suggested by Dr. R. T. Ross. The surgery was performed by Dr. D. Parkinson.

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CAROTID ARTERY THROMBOSIS

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THROMBOSIS of the internal carotid artery is a major factor in the sudden occurrence of hemiplegia in patients 45 years of age and older. Recent specific clinical and autopsy investigation suggests that it is found in approximately 25% of cases if it is properly looked for. It is generally considered to be a disability of the upper age-group but the literature reports at least 17 cases in patients under the age of 15 years. The cases reported in the upper age-group suggest atherosclerosis as the basic factor, but as in other arteries the process may well be localized. Trauma may play a role in both age-groups but more particularly is it suspected in the younger age-group. The importance of carotid angiography in aiding a specific diagnosis in the "stroke syndrome" scarcely needs emphasis. Internal carotid thrombosis, berry aneurysms and tumour may be discovered, and these patients may obtain surgical help.

Mr. G.L., a 49-year-old man who had previously been in excellent health, developed rather sudden numbness in the fourth and fifth left fingers on December 31, 1958. This numbness persisted and he found it awkward to do things with his hand and to get his hand into his pocket. He was examined by an internist who could find no apparent reason for his disability. He was seen by the writer in February 1959, at which time the Adson test was negative and there was no evidence of costo-brachial syndrome. There was, however, a small calcification at the top of the ulnar groove (Fig. 1), and it appeared that the trouble with his ulnar nerve was coming from this region. Radiographs of the neck at that time revealed narrowing between C5 and C6, suggestive of cervical disc disease, but it did not involve the eighth cervical or first thoracic. A diagnosis of secondary ulnar neuritis was made; he was admitted to hospital and the ulnar nerve was dissected free from some calcified material in its groove, and transplanted.

After this procedure he recovered slowly but steadily, and sensation returned in his fourth finger and somewhat in his fifth. On May 3, 1959, he experienced a sudden loss of extensor power in his left hand, associated with some weakness of the left side of his face and numbness of the whole back of the hand. After this episode he developed atrophy of the small muscles of the hand, but over the next four weeks some extension at the wrist and fingers returned. Five weeks later, while climbing a ladder, he noticed weakness and subjective numbness in the left leg. Shortly he developed numbness and weakness of the left side of his face and had difficulty with movements of his tongue. He was advised to enter hospital for angiography, but because of his hesitancy and the difficulty in obtaining a bed this was not accomplished for several weeks.

By the time of admission he had developed a moderate degree of facial shift to the right, his left arm swung limply at his side and he dragged his left leg.



Fig. 1.—Calcium fleck at the entrance to the ulnar groove of left elbow.

Carotid angiography (Fig. 2) revealed a complete block of his right internal carotid artery just beyond the bifurcation of the common carotid (the location of approximately two-thirds of these lesions).

Although this lesion was complete (best results are obtained in cases of stenosis), an arteriotomy was performed on July 15, 1959. There was a pea-sized thrombotic plaque at the area indicated in the angiogram. This was removed and adequate circulation occurred from the proximal artery. However, the distal artery did not bleed satisfactorily even after insertion of a ureteral catheter through the carotid canal and flushing it with heparin solution. The artery distal to the block was collapsed and soft and possessed an adequate lumen. The arteriotomy wound was then closed and the internal and common carotid arteries were stripped of their adventitia from the carotid canal to the suprasternal notch.

Anticoagulants were administered and within 24 hours the subjective and objective disabilities in his left leg improved dramatically. Within one month the



Fig. 2.—Carotid angiogram showing complete block of the internal carotid just distal to the bifurcation of the common carotid artery.

patient's walk had changed from that of a typical partial hemiplegic to a normal gait. The improvement in his left arm was less rapid, and although extensor power of the wrist and fingers improved slowly, considerable atrophy of the intrinsic muscles of the hand became apparent. Six months later his gait was normal. His face was normal in appearance and function. But even with good extensor power in his wrist and fingers there is still moderate atrophy of the intrinsic muscles of the left hand.

It is possible that his early complaints, diagnosed as secondary ulnar neuritis, were attributable to early stenosis or block of the right internal carotid artery.

SUMMARY

A case of thrombosis of the internal carotid artery with arteriotomy and almost complete recovery has been presented. The frequency of these lesions has been suggested. The importance of making a specific diagnosis by carotid angiogram in the so-called stroke syndrome has been indicated.

SHORT COMMUNICATIONS

THE END OF AN ERA

H. M. HARRISON, M.D., *Toronto*

THE MEDICAL profession of Canada has been made aware of the fact that the Canadian Medical Institute will cease operation June 30, 1960. As physician in charge of the Institute since it was founded in 1931, I have been asked to outline its history briefly and to give some observations on its operation.

The first association of the profession in regard to periodic health examination and the insurance companies was in 1930. The suggestion that the insurance companies should aid in the promotion of periodic health examinations was made in 1927, in a letter by Dr. R. E. Wodehouse, then secretary of the Canadian Tuberculosis Association, to the late Mr. V. R. Smith, general manager of the Confederation Life Association.

Correspondence was carried on between the health committee of the Canadian Life Insurance Officers Association and Dr. Clarence Routley of the Canadian Medical Association, from that date until 1930, when a periodic examination program under the auspices of the Canadian Medical Association functioned for one year. Then, with the blessing of the C.M.A., three of the insurance companies, namely, Sun Life Assurance Company, The London Life Insurance Company and Confederation Life Association, founded the Canadian Medical Institute. Credit must be given to the founders, Mr. E. E. Reid, Mr. V. R. Smith and Mr. A. B. Wood, who gave of their time and enthusiasm to see the Canadian Medical Institute through its

first five years. In 1946 the North American Life Assurance Company was admitted to membership.

The idea the founders had in mind was two-fold: firstly, to educate and encourage the policyholder to have a physical examination regularly, and secondly, to encourage the policyholder to maintain contact with his family physician.

The first objective we feel has become well accepted. Today, through their place of employment, many people are regularly receiving periodic examinations, and the various provincial tuberculosis associations have definite programs of regular x-ray examination. With respect to the second objective, our surveys show that between 75% and 80% of our examinations were carried out by the family doctor.

Since commencing operation in 1931, we have completed over 260,000 examinations. This has undoubtedly played an important part in educating the public to such a procedure. After directing this service for 29 years one naturally has some opinions on the value and on the shortcomings of such a service. The most emphatic statement I can make is that this examination should be performed by the family physician. The laity are too prone to self-diagnosis. Further, the specialist would much rather have a referred patient than one coming in on his own. The annual examination keeps the family doctor in touch with his patient. This enables him to carry out appropriate preventive measures.

I would like to comment on the changed attitude of the medical profession towards periodic health examination. At first there was definite antagonism by a minority towards these examinations, particularly some of our elder statesmen. I well remember at a meeting of the Ontario Medical Association in London in the mid-thirties, a former senior officer of the Association who publicly ridiculed the whole idea. Today that has changed. The profession is convinced that periodic health examination is a useful preventive measure.

One remark heard occasionally, generally from people who know little about the subject, is that periodic health examinations make neurotics of some of those examined. In addition to the work in the Canadian Medical Institute, I have been conducting periodic examinations for the last 25 years for employees in five industries in Toronto. I can positively state that this accusation is without foundation—any person who is a neurotic after an examination was a neurotic before.

As to the findings of periodic health examinations, the most common disease is obesity. Our experience is that the majority try to reduce and many are quite successful. Thirty years ago the profession paid little attention to this condition. At present it is rare for an examiner not to caution a man about his weight, where such advice is indicated.

The Institute's examination form stresses the need for the physician to question carefully regarding

any change of function which might indicate the presence of an early malignancy. It has been said that the family physician is the best, and, in many areas, the only cancer clinic, and that by his careful examination and search for signs and symptoms suggestive of early malignancy, a definite reduction in the cancer death rate is possible. At the best of times it is difficult to determine the presence of such a condition, but from a recent study of the records of some 2000 consecutive examinations we learned that 3% were advised by their examiner to have a complete gastro-intestinal investigation because of some obscure symptom.

A prominent urologist wrote me stating that he had recently operated upon two patients with early prostatic carcinoma, both discovered through periodic health examinations by the Canadian Medical Institute. He stated that in each case the prognosis was good.

An interesting sidelight on periodic health examinations is given in an article in the *Journal of Postgraduate Medicine* (March 1960) by Dr. Roger Baker, "Approximately 12,000 men die each year from prostatic carcinoma, yet in about 90% of the patients this malignancy begins in the area of the prostate that is palpated at the time of rectal examination. Strangely enough, only 5 to 10% of the patients with carcinoma of the prostate are referred to the urologist early enough so that radical surgery can be attempted. There are two possible reasons for this. Not enough periodic examinations are done on men over the age of 45 years, and physicians are not completely familiar with the digital characteristics of early carcinoma of the prostate."

Glycosuria was detected in over one in every 100 examinations of the urine. A few of these were proved to be of renal type, but the percentage was small.

Some years ago we studied the records of 500 persons who died of coronary artery disease and who had been examined within two years of death. In 85% one or more of three findings were noted: overweight, 10% or more; abdominal girth greater than girth of chest on inspiration; and hypertension of 140/100 mm. Hg or greater.

Further examples of the value of periodic health examinations could be given, but I would like instead to repeat a conversation I had with a prominent physician in western Ontario. We were discussing experiences when he mentioned that during the last year he had detected three cases of early breast carcinoma by periodic examination. All had been operated upon, and in all the prognosis was excellent, owing to early detection.

In closing, I would like to thank the medical profession of Canada for their interest and co-operation in the work of the Canadian Medical Institute over its 29 years of operation.

ANTIMALARIAL COMPOUNDS IN RHEUMATOID DISEASE

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OBSERVATIONS on the use of antimalarial compounds in rheumatoid disease continue to appear in the medical literature with sufficient frequency to warrant a further attempt to assess their value in the long-term management of this chronic and vacillating disease.

Until, or unless, a cure be found for rheumatoid disease (which is extremely doubtful, as it seems to be a systemic upset that certain individuals manifest upon exposure to sufficient stress of an appropriate type), the ideal drug would be one that is effective in the majority of those afflicted, and of such low toxicity that it can be given, in an effective dosage, for as many years as may be necessary to control the disease process in any given patient. This concept involves the "chronic toxicity" of such a drug just as much as, or probably more than, its effectiveness.

At this, the end of the first decade, the daily use of cortisone-type steroids has been shown to be too hazardous when continued for years to be worth the risk in all except the worst cases (which amount to no more than about 10% of those afflicted). Long-term phenylbutazone (Butazolidin) treatment, while still hazardous, is safer (if well tolerated for three to six months) but is effective in less than 50% of those with classical peripheral rheumatoid arthritis, although it may well be the drug of choice for the long-term control of rheumatoid spondylitis.

For a variety of reasons, and although quinine is of no value, the antimalarials have been employed for rheumatoid disease since 1951. After the "lead" in the treatment of discoid lupus, quinacrine (Atabrine, Mepacrine) was first employed but was discarded, because of chronic toxicity, in favour of chloroquine (Aralen, Resochin). More recently, hydroxychloroquine (Plaque-nil) has received fairly extensive trial because, at least in the same range of dosage, it is even less toxic than chloroquine. Amodiaquin (Camoquin, Miaquin) is also under study.

All published papers indicate that chloroquine has the property of inhibiting rheumatoid disease to a variable degree in the majority of patients. Its therapeutic position has been somewhat confused, however, by variation in dosage used and therefore in the findings of acute and chronic toxicity reported. It now appears that most patients cannot tolerate more than 250 mg. of chloroquine diphosphate daily for long periods of time but that, if tolerated, 250 mg. is an effective dosage in 50% or more of patients.¹ Lesser doses may be just as effective in some adult patients, and in juveniles. Doses of 500 mg. or more daily result in a high incidence of gastro-intestinal side effects that are

not, however, of the "hyper-acidity dyspepsia" type in that they do not respond to ulcer-type therapy, but only to reduction of dosage, or withdrawal, of the drug. In doses of 250 mg. daily (or less), only two side effects appear to be significant. The "seasickness" syndrome appears early, is apt to be transient, and may require only temporary withdrawal or reduction in dosage. It is responsible for permanent cessation of therapy in only 4% of patients. Drug dermatitis, on the other hand, is usually late in appearing (any time from six months to four years) but requires permanent withdrawal of chloroquine in almost 15% of those treated for one or more years. Rarely, it may appear early. Leukopenia has been noted but always with a normal differential count, and agranulocytosis has not occurred even when chloroquine is continued in the face of leukopenia.

When hydroxychloroquine sulphate (Plaquenil) became available (in temperate climates, about 1956), it was tried as an alternate to chloroquine in the treatment of rheumatoid disease because gastro-intestinal intolerance and seasickness were much less frequently observed in comparable mg. doses in the treatment of malaria, amœbiasis and discoid lupus. It too appears to be effective^{2, 4} in a majority of patients with rheumatoid disease, but it has been found necessary to scale the dose upward to achieve the same results as are obtained with chloroquine. The dose of hydroxychloroquine must be at least 400 mg. daily, and possibly even 800 mg. daily, to make it as effective as 250 mg. daily of chloroquine. A dose of 400 mg. daily of hydroxychloroquine is rather better tolerated for long-term use than 250 mg. of chloroquine, but it appears that when equipotential anti-rheumatoid dosage is approached, the toxicity evens out. Much more is known of chronic toxicity of chloroquine in reference to dosage, however, than there is of hydroxychloroquine because the former has been available so much longer.

To summarize the present position in regard to chloroquine and hydroxychloroquine, perhaps it is significant that those with the largest published experience with these agents in the treatment of rheumatoid disease, Bagnall¹ and Scherbel,³ have sufficient confidence in their effectiveness, and have encountered a sufficiently low incidence of toxicity to take them into routine use in the treatment of rheumatoid disease. On the other hand, chloroquine will not be effective enough in one-third or more of the patients (particularly if they have been on long-term glucocorticoid cortisone-type therapy previously) and 15 to 20% of those who originally show a very good response to chloroquine may have to stop it eventually because of toxicity. Of those who have to stop chloroquine, 25% cannot tolerate effective doses of hydroxychloroquine either, and another 25% fail to maintain their gain on hydroxychloroquine unless a large dose is used, which again increases the long-term chance of toxicity.

During the past two years, a minor "bombshell" has been thrown at the antimalarial therapy of rheumatoid disease—English investigators have reported significant slit-lamp evidence of eye toxicity from chloroquine, hydroxychloroquine and amodiaquin (Camoquin, Miaquin). This latter compound is, like chloroquine and hydroxychloroquine, a synthetic 4-aminoquinoline that appears to have anti-rheumatoid potentialities, but has had much less extensive field trials than the other two. Kersley and Palin⁴ confirm the 1958 reports of Hobbs and Calnan,⁵ and Zeller and Deering,⁶ that these anti-malarials may give rise to microscopic corneal opacities of specific type, without necessarily resulting in a corresponding amount of visual loss. The report of Kersley and Palin indicates that there is a definite correlation between the level of dosage and the extent of the corneal lesion, and that the latter gradually cleared on withdrawal of the antimalarial therapy. Earlier reports, even those made as a result of a large experience, did not mention anything but blurring of vision that occurred rarely and was attributed to difficulty in focusing. Kersley and Palin employed a rather large dosage and were particularly alerted to seek for such corneal changes but re-examination of data by earlier authors^{2, 7} on the chloroquines has failed to indicate that irreversible serious eye changes were missed.

To put the phenomenon of toxic posterior keratitis in proper perspective, a review of the experience⁷ of the Cleveland Clinic group may be mentioned. Among 1500 patients treated with one or other of the chloroquines for more than one year, and up to five years, only five cases with "typical" corneal involvement have been encountered and these have all subsided completely on withdrawal of the drug. It has not altered their favourable opinion of the value of these drugs for rheumatoid arthritis and related disorders. In a smaller experience, extending over an even longer period of time (seven years), Bagnall² has found no instance of visual loss of this type that required ophthalmologic consultation. Blurring of vision occurred in three patients, but subsided with reduction in the dose of chloroquine in two and switching to hydroxychloroquine in the other. Nevertheless, the eye should become another focus of search for toxicity in those patients receiving long-term antimalarial therapy in the dosage used for rheumatoid disease and lupus erythematosus.

Another English report⁸ of three cases of retinopathy in patients receiving chloroquine therapy stimulates less concern because the element of coincidence seems high in proportion to the absence of such clinically obvious lesions in previously published reports dealing with a large experience with this drug and its congeners.

Special mention should be made of the latent period of action of the antimalarials in rheumatoid disease. In one series⁹ of 150 patients, with continuous use of the chloroquines for at least one

year and up to five years, major benefit accrued in 100 patients. In those with *major* benefit, minor objective benefit did not occur in all until almost four months, and major benefit was delayed until eight months, on the average. Remission (under continued treatment) occurred in almost half of those with major benefit but was delayed for up to ten months or more. Use of an early large dose hastened toxicity and did not seem to improve results in the long run, particularly with chloroquine, but it seems clear² that about 400-600 mg. daily of hydroxychloroquine must be used as an alternative to 250 mg. of chloroquine and that then the toxic side effects approach equivalency. On the other hand, relatively small (200-400 mg. daily) doses of hydroxychloroquine may be effective when effective doses of chloroquine are impossible to maintain because of dermatotoxicity.

SUMMARY OF DRUG THERAPY IN RHEUMATOID DISEASE

Chloroquine diphosphate (Aralen, Resochin) 250 mg. daily, or long-term hydroxychloroquine sulphate (Plaquenil), in twice the dosage, appears to be the drug of choice for the routine long-term treatment of rheumatoid disease when effectiveness and absence of toxicity are both taken into consideration. Transient, or intermittent, oral or intra-articular hydrocortisone-type therapy is a useful adjunct to bridge the gap of the long (two to six months) latent period of antimalarial drug action, but preceding continuous oral long-term cortisone-type therapy militates against the effectiveness of the antimalarials. The place of a third and perhaps more toxic 4-aminoquinoline synthetic, amodioquin, is not yet satisfactorily assessed, but all the rest of the antimalarial congeners are either too toxic for chronic use or, like quinine itself, ineffectual.

Because of greatly reduced toxicity and apparent similarity of action, the chloroquines appear to have replaced the use of gold in the long-term management of classical rheumatoid arthritis of peripheral joints. The chloroquines also probably replace continuous cortisone-type treatment, although cortisone-derivatives may be a useful *temporary* adjunct and intra-articular injection of hydrocortisone, or its derivatives,

may be very valuable indeed to cover the latent period of three to ten months before the antimalarials are maximally effective.

Usefulness of phenylbutazone (Butazolidin) is not denied, but this drug is considered more hazardous and less effective in the long run on the average than are the chloroquines, with the exception of rheumatoid spondylitis in which phenylbutazone appears to be the drug of choice.

No discovery in the past 25 or 50 years has served to replace acetylsalicylic acid as the best single anti-rheumatic *symptomatic* measure. It may be necessary, however, to employ the much more expensive "buffered" forms (Disprin, Paynocil, Bufferin) or enteric-coated preparations (Entrophen, Ecotrin) to achieve a dosage adequate to control symptoms and, at the same time, avoid gastric irritation. Probably because of this factor of gastric irritation, most rheumatoid patients today still receive far less than an adequate dosage of acetylsalicylic acid, which should be at least 60 grains (4 g.) daily and up to 100 grains, if tolerated. Whatever else is used, provided gastric irritation is not produced, maximum tolerated doses of salicylates will reduce the toxicity and the dosage of any less conservative adjunct therapy, such as continual administration of glucocorticosteroids.

Only intra-articular hydrocortisone (or one of its derivatives) is as safe and effective an adjunct as acetylsalicylic acid in the majority of rheumatoid patients, and should be employed much more than it is for those patients in whom inflammation of one or a few joints is forcing the physician to consider more radical measures, such as continuous phenylbutazone, or continuous glucocorticoid, or parenteral gold, therapy.

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CANADIAN JOURNAL OF SURGERY

The July 1960 issue of the *Canadian Journal of Surgery* will contain the following original articles, case reports, surgical technique and experimental surgery:

History of Canadian Surgery: Manitoba surgical pioneers—Ross Mitchell.

Original Articles: Esophageal stricture secondary to hiatus hernia in the aged—E. M. Nanson. Islet-cell tumours of the pancreas—J. R. F. Mills. Adrenal carcinoma—J. E. Leddy, L. M. Brand and K. J. Postma. Carbon dioxide narcosis in the postoperative period—R. J. Baird and W. G. Bigelow. The flexure syndrome: relationship of bowel angulation to obstruction—W. R. Ghent. Benign gastric tumours of non-epithelial origin—J. Couture. Measurement of brain circulation time by radioactive iodinated albumin—W. Feindel and S. Fedoruk. Primary retroperitoneal tumours—J. K. Wyatt and L. N. McAninch. Developmental coxa vara—H. R. Carter.

Case Reports: Grease-gun injury—J. C. Osborne. Transpyloric prolapse of aberrant pancreatic tissue—J. D. Longley and R. W. Boyd. Mesenteric lipoma in children—W. L. Ogilvy.

Surgical Technique: Further studies of catheter-venous sets employing half-needle guide—E. C. Elliot. Disinfection of anaesthetic apparatus—P. Warner and J. Doherty.

Experimental Surgery: Morphological changes in the liver and biliary tract of dogs with partial obstruction—A. C. Richie, F. G. Murphy, D. R. Webster and S. C. Skoryna.

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(Information regarding contributions and advertising will be found on the second page following the reading material.)

ETIOLOGY OF PSYCHOSOMATIC DISEASE

Suburban living is becoming the accepted form for ever greater numbers of city dwellers. In the United States 12.4 million people were added to the suburbs from 1950 to 1958.¹ The rate of increase of the suburbs was three times the rate within the cities to which they are adjacent and more than double that of the United States as a whole. This is even more striking when we learn that some of the larger cities of the United States have in the same period grown only very little or not at all. Boston has had a decrease of population (1% per annum) and so have Pittsburgh and Providence, whilst New York City, Newark and Jersey City have shown no appreciable change. Their adjacent communities have at the same time been growing at the rate of 3.9% a year. Because of this suburban growth, the population of the metropolitan areas in the U.S.A. rose in 1958 to 59% of the total population of the country (56% in 1950).

It is obvious that such rapid growth of communities is bound to affect inhabitants in various ways, and sociologists have been warning us of its hazards. Gordon and Gordon² report a study on the prevalence of psychosomatic diseases in rapidly growing suburbs. Hospital admissions for asthma, coronary thrombosis, duodenal ulcer, essential hypertension and hypertensive cardiovascular disease were compared in three hospitals with the admissions for bronchopneumonia in the period of 1950-1951 and 1957-1958. The three hospitals were located in a rapidly growing suburb, a mixed rural community, and a stable rural area respectively. The results of this statistical study show a significant difference in the incidence of various diseases in the three hospitals. There was a higher percentage of admission of tension disorders to Englewood Hospital, serving a rapidly growing suburb, than to the other two. Asthma was more prevalent in the hospital serving a rural community with a high percentage of old people. "They are being

left behind there, are without adequate activities and are often quite depressed."

We are all aware of the present popularity of "psychosomatics" in both medical and lay circles, and it is not as difficult as it used to be to convince a patient that his disease is primarily in his "mind" and not in his "body". But that does not prove that the illnesses which are ascribed to emotional disorders are psychosomatic diseases. Let us remember that some 130 years ago general paralysis of the insane was regarded as the psychosomatic illness *par excellence*, the exact opposite of the present-day concept.

In a lecture to the Zurich Medical Association Bleuler³ stresses the difficulties of proving the purely emotional etiology of the so-called psychosomatic diseases. According to him, the well-known effects of emotion on bodily function do not prove that organic disease is actually caused by emotional disorder. Bleuler is a psychiatrist, who had initially been a general practitioner and a surgeon, and his observations are obviously based on personal experience. He welcomes continued investigation of the mechanisms by which emotional disorders can produce physical illness, but he points out that when one states definitely and accepts as proven that the above diseases are caused by emotional disturbance, one has left solid scientific ground and is in the realm of speculation. Somatic manifestations of psychiatric diseases must be sharply separated from the conditions under discussion and cannot serve as proof by analogy. The fact that we have no evidence of impersonal, extra-corporeal etiological agents of these diseases does not exclude our finding such at a later date. Human beings explain even impersonal events in a personal way, and it is not surprising that bodily illness is blamed on a mental distress. Uncovering of connections between inner experience and manifestations of illness makes assumption of psychosomatic disease plausible and possible, but does in itself not prove it. Psychotherapeutic success has indeed been achieved temporarily in many cases, but prolonged cures have been few and not sufficiently well documented by objective, sound medical observation. Bleuler sees danger in the vagueness of the concept of psychosomatics. It allows us to imagine the connections between psyche and somatic functions in any way we like and to have many misconceptions that are harmful to progress.

Although it has to be admitted that the present trend towards acceptance of psychosomatic medicine has promoted a more comprehensive approach to the patient and his illness, the empirically minded physician cannot rid himself of a sense of discomfort. The discussion by Gordon and Gordon of the reasons for the differences in the three communities sounds logical and their explanations are ingenious. Maybe the unaccustomed language of psychosomatics is incomprehensible to some of us. Or is it the lack of a sound, philosophical

basis? Perhaps the methods applied in this field are so radically different from those used by natural sciences. One may question whether the rate of admission to hospitals can be considered a true yardstick for the incidence of disease. As neither asthma nor peptic ulcer are diseases for which most patients are admitted to hospital, one could argue that an increased rate of admission merely indicates a more severe form of the diseases.

Will such studies be able to take all possible factors into consideration? Will they establish the etiological relationship between "modern high-pressure living" with its resulting emotional strains and stresses, and gastric hypersecretion, hypermotility and ulcer, or hypercholesterolaemia and coronary artery disease? Is it really as simple as that?

W. GROBIN

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Editorial Comments

GRISEOFULVIN: AN APPRAISAL

The deluge of papers¹⁻⁹ on griseofulvin makes some critical evaluation and condensation seem mandatory to establish a rational basis for the use of this new antifungal antibiotic in superficial fungous infections.

Keratin is made up of closely packed polypeptide chains held together by disulfide bonds of cystine. It is resistant to solvents and enzymes. The nails, hair cortex and cuticle are made of hard keratin; the stratum corneum of the epidermis and hair medulla are made of soft keratin. Superficial fungous infections are a parasitic infection of keratin; the fungi live in, feed on, distort and destroy keratin. Some fungi cause an acute inflammatory reaction which is self-destructive: the inflammation casts off or destroys the fungi or keratin. It should be noted that these are self-healing conditions. Those fungi which cause only a mild reaction frequently give rise to a chronic low-grade infection. The basic reason for individual susceptibility is not known. Some of the known conditioning factors are heat, moisture (tinea pedis), obesity, diabetes mellitus (moniliasis) and Cushing's syndrome¹⁰ (*Trichophyton rubrum* infections). The basis for treatment prior to griseofulvin was a peeling off of invaded keratin by ointments (Whitfield's ointment) or x-ray epilation. This was curative in some cases and helpful in others. However, in many cases the anatomy of the skin appendages (e.g., hair and sides of nails) made thorough peeling impossible, and so the invaded keratin was never completely removed.

Griseofulvin was isolated in 1939 from the mould *Penicillium griseofulvin*. It was used successfully in

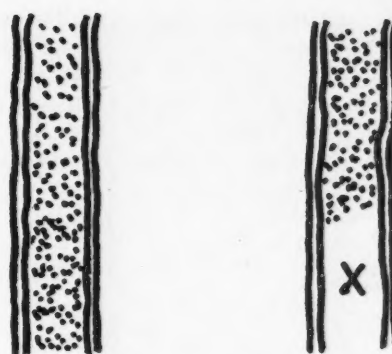


Fig. 1.—Diagram of cross-section of human hairs infected by *Microsporon canis*. X marks the proximal portion of the hair where the griseofulvin-containing keratin has no fungal products. (After A. R. Birt *et al.*⁶)

the treatment of fungous diseases of plants and guinea pigs before Williams, Marten and Sarkany² reported its successful use orally in human ringworm. The drug is absorbed from the gastro-intestinal tract into the blood stream, from which it is deposited into the growing keratin of the skin and hair. Fungi do not grow in griseofulvin-containing keratin (see Fig. 1). We can postulate the development of a griseofulvin shield which slowly extends into the non-living keratin of the nails and hair. This antibiotic is fungistatic, and the rate of cure will depend on the rate of growth.

Keratin source

Time for response

Skin	1 week
Hair	5-6 weeks
Nails: Finger	5 months
Toe	9 months or more

Griseofulvin must be given continuously because re-infection may occur from the tips of infected hairs not infiltrated with the drug or from the keratotic subungual debris in the nails.

Many problems about the practical therapeutics of this drug are not yet understood. The following material is based on a thorough study of what has so far come to light. As with all medical practice, an accurate diagnosis is essential. Clinically, even the most expert student of morphology can be led up the garden path unless there is confirmatory laboratory evidence of fungous disease. This evidence may be obtained by examination under the microscope of skin scrapings or hair soaked in 15% KOH, by culture on Sabouraud's medium or by examination under an ultra-violet (Wood's) light. Most provincial health departments provide these services free of charge. Therapeutic trial of this powerful specific drug are to be condemned. A superficial fungous disease is not an emergency. The daily oral dose in children up to 12 is 25 mg./kg., in adults 1.0 g. The drug is not effective topically. Griseofulvin is the drug of choice in those superficial fungous diseases most resistant to peeling agents and those least influenced by conditioning factors. *Trichophyton rubrum* is a chronic low-grade infection of the nails and skin. Prior to griseofulvin there was no effective treatment. *Microsporum audouini* (human non-inflammatory) scalp ringworm was satisfactorily treated only by x-ray epilation,

and a very occasional accident with permanent loss of hair did occur. Other more rare tinea such as favus respond remarkably. It may be indicated in some cases of garden-variety tinea, viz. tinea pedis, cruris and corporis, but usually these respond to conventional therapy. Griseofulvin is not indicated in self-limited animal inflammatory ringworm (kerion). Already there are reports in the literature of cures in from 7-9 weeks⁵; the authors have forgotten that in this time inflammatory ringworm will be gone almost no matter what you do,^{6, 11} and at 25¢ a pill the patient will be about \$55.00 richer. Resistance has been reported in the test tube, but not *in vivo*—or perhaps one should say not yet. No specific toxic features are present. Moniliasis of intertriginous areas has been reported during and following griseofulvin treatment. Healthy carrier states (cf. typhoid bacilli, staphylococci) do occur. Conventional therapy in the form of peeling agents and the avoidance of conditioning factors such as heat and moisture should not be neglected. Re-infections do occur "because the patient is susceptible to fungous disease."

This is truly a remarkable advance in therapeutics. If used judiciously and intelligently, much suffering will be alleviated. Perhaps also we can hope that this drug will halt the chronic diarrhoea of topical antifungal agents, each one of which, like the detergents advertised on television, is better than the next, and none of which is any better than Whitfield's ointment. ROBERT JACKSON

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DRUG REACTIONS

A comprehensive discussion of common drug reactions is provided by Criepp of Pittsburgh, Pennsylvania, in a recent issue of *Connecticut Medicine* (24: 94, 1960). The various types of reactions are described and case reports to illustrate them are included. The severity of the reaction varies from angioedema due to sulfathiazole, and contact dermatitis due to a variety of drugs including pilocarpine and streptomycin, to exfoliative dermatitis due to penicillin, quinidine, and iodine. Agranulocytosis and leukopenia may well be due to the particular drug's combining with white cells and thus rendering them antigenic. Production of anti-leukocytic antibodies stimulated by this antigen follows, and their union with white blood cells causes their destruction.

The best way to treat drug reactions is to prevent them by avoiding the use of drugs whenever possible. Antihistaminics given along with a drug

that may be sensitizing the patient are of doubtful value. People who are allergic to such drugs as penicillin or to horse serum should perhaps carry identification tags containing this information. The results of sensitization tests are variable and, in the author's experience with antibiotics, a negative skin test does not exclude the possibility of subsequent reaction. A positive test, however, makes the appearance of such a reaction more likely.

In conclusion, Criepp states that the rising incidence of drug reactions and the occasional severe and even fatal outcome indicate need for caution and conservatism in the use of drugs. Early recognition of a reaction is essential in order to prevent serious outcome. In general, unnecessary employment of antibiotics and other therapeutic agents is not only wasteful but dangerous. W.G.

"IT'S THE TIME-FACTOR"

In a recent lecture series in Toronto, Jacques Barzun spent considerable time criticizing the social scientists who, he claimed, are primarily interested in predicting and ultimately controlling human behaviour to their own or others' nebulous ends.

He gave an interesting example *en passant* of the effect of one of the assumptions of the social sciences, that man has no free will, in our present way of living. This assumption leads to thinking of behaviour in terms of drives and forces completely beyond the control of the individual. The example was that of a housewife on the telephone who says to her caller, "No, I won't be able to do that. It's the time-factor." This woman visualizes herself as caught up in a confusion of forces and factors that she cannot get around. Compare her, on the other hand, with one whose time is spent perhaps doing the identical things and who yet says on the phone, "No, I can't come. I don't have time." Here there is no cloud of compulsion and slavery. This woman chooses to do whatever she is doing and simply recognizes that she has no time for anything else, but with no feeling of being driven.

The latter views herself as a human being who feels free to choose what she will; the other housewife sees herself as a machine operating under a time-factor and valued in terms of her output.

In this regard, we can see that the social scientists who, in their denial of human freedom, are seeking to predict and control humankind, are most satisfactorily refuted by a determination on our part to hold on to our freedom and do what we choose.

It is because we are free that we are able to give up our freedom to become slaves to an idea, an institution, or a government. It is within our power to withhold our assent from what we judge to be a form of slavery, in which the labourer is *not* actually treated as worthy of his hire. In our present system of free enterprise, therefore, we might well uphold as a suitable motto that "the labourer is worthy of his hire".

Medical News in brief

NUTRITION AND OLDER PEOPLE

In a recent article in the *Canadian Journal of Public Health* (51: 101, 1960), McHenry emphasizes that very little good information is available regarding nutritional requirements in the aged. He related that a senior clinical colleague came to him and stated, "There is a great amount of protein deficiency among elderly people in this city. What are you doing about it?" McHenry asked how he knew there was so much protein deficiency. The reply was, "There must be—the people are living on tea and toast." But such a statement is not backed up by any facts.

Since it has become fashionable to sponsor discussions on geriatrics, it might be more useful to obtain basic information necessary for intelligent discussion. For example, how much protein do elderly people need to maintain balance and to prevent wasting? What is the efficiency of digestion and absorption of such nutrients as protein, calcium and iron in elderly persons? And what are the nutritional problems among elderly people and how prevalent are they?

Until this knowledge is available, physicians can do no better than use the Canada Food Rules as a guide. As well, they can help greatly by dispelling notions about the harmfulness of certain foods, such as meat, cheese, milk and acid fruits. Further, elderly people should be encouraged to eat meals which they enjoy rather than to accept meals which are believed nutritionally adequate: the objective being, by tact and proper planning, to have them eat meals that are nutritionally adequate and pleasant at the same time. Finally, special diets, particularly low sodium diets, should not be indiscriminately prescribed for elderly people but only when there is evidence to warrant their use.

METABOLIC RESPONSE TO CRANIOCEREBRAL TRAUMA

During recent years valuable contributions have been made to our understanding of metabolic deviations following bodily trauma, mainly through balance studies, and it seemed logical to McLaurin *et al.* (*Surg. Gynec. & Obst.*, 110: 282, 1960) to apply the technique to patients with head injury. Data were obtained from a study of 11 patients who had moderately or markedly severe brain injury, minimum or absent associated bodily injury, and no known pre-existing metabolic disturbance.

The most consistent metabolic effect noted was a nitrogen loss which was often quite large and seemed to be unrelated to nitrogen intake within certain limits. The negative balance was usually in the range of 10 grams per day, corresponding to a loss of approximately 300 grams of muscle tissue daily. Three patients with fractures of bones had an average net loss of 11 g. of nitrogen daily; thus the effect of associated injury was minimal in this regard. Nitrogen feeding during the period of post-traumatic catabolism was not accompanied by significant improvement of negative nitrogen balance.

Sodium retention did occur but usually lasted only from two to three days, and was not as great as has been noted after major abdominal surgery. In all patients on whom the study was continued for 10 days, sodium equilibrium was restored. Potassium metabolism, on the other hand, was not significantly affected. There was no period of negative balance to correspond with sodium retention.

Water balance is exceedingly difficult to evaluate because of extra-renal losses. Disregarding such losses, the cases studied showed a positive balance varying between 500 and 1500 c.c. daily with an average of 1100 c.c.

The rational form of nutritional support of such patients then would be as follows: Administer fluid volumes of 2000 c.c. during the first few days. Begin salt administration in amounts of five to 10 grams daily. No administration of extra potassium is necessary. Because utilization of administered nitrogen is very inefficient in the injured patient, protein should not be given in amounts greater than one gram per kilogram of body weight. Simultaneously, the total fluid intake should be increased to about 3000 c.c. daily. In general, there is probably greater danger in starting tube feedings too early than in delaying for several days.

GENETICS OF CONVULSIVE DISORDERS

Studies designed to investigate hereditary factors in various epilepsies have been in progress at the department of genetics, McGill University, and at the department of medical genetics, the Montreal Children's hospital, since 1951. In an introductory report Metrakos and Metrakos (*Neurology*, 10: 228, 1960) discuss the difficulties inherent in studies of this kind, particularly in trying to determine the importance of heredity versus environment and, in studying groups of people, separating the affected from the unaffected. The question: Is epilepsy hereditary? is examined from the geneticist's point of view.

The study involves 1000 consecutive admissions to the Montreal Children's Hospital, and in this group 115 patients were found to have had at least one convulsion in their life. Sixty-eight of these patients were selected at random and their family histories obtained. This necessitated investigation of 20 classes of near relatives of each proband. An identical pedigree study of 132 of the 885 admissions without history of convulsions was carried out to serve as a control.

The authors suggest that the genes responsible for convulsion may be divided into three major categories: threshold genes, cerebral disease genes, and "epilepsy" genes. Expressivity, penetrance and chronicity may determine the degree to which the genes will influence the person in question.

It was found that the prevalence of near relatives with at least one convulsion was 2.9 times higher in the "convulsion" group than in the control group, and this difference was statistically significant. From this and other data that are presented it is strongly suggested that a familial distribution of convulsions is present; however, the distribution is apparently not uniform throughout the families.

(Continued on advertising page 29)

NEW DRUGS

This listing of new products is based on information received from Dean F. N. Hughes, Faculty of Pharmacy, University of Toronto, and the *Canadian Pharmaceutical Journal*, to whom we owe thanks.

PSYCHOTHERAPEUTIC AGENTS

Nialamide: NIAMID (Pr), Pfizer

Description.—Scored tablets containing 25 mg. (pink) or 100 mg. (orange) nialamide, antidepressant.

Indications.—Emotional fatigue, depression, excessive worry, hypochondria, etc.; useful in patients with neurotic and psychotic syndromes.

Administration.—Initially, 150 to 200 mg. daily in divided doses. Adjustments to be made according to response at intervals of 7 to 10 days.

How supplied.—25 mg. tablets, bottles of 30 and 100. 100 mg. tablets, bottles of 100.

LIBRIUM (Pr), Roche

Description.—Each capsule contains 10 mg. of 7-chloro-2-methylamino-5-phenyl-3H-1, 4-benzodiazepine 4-oxide hydrochloride, as psychotherapeutic agent.

Indications.—In low doses: mild to moderate anxiety and tension, tension headache, premenstrual tension, apprehension, etc. In higher doses, for severe anxiety and tension states, agitated depression, chronic alcoholism, etc.

Administration.—Mild to moderate: 10 mg. 3 or 4 times daily (children, once or twice daily). Severe anxiety and tension: 20 mg. 3 or 4 times daily.

How supplied.—Bottles of 100 and 500.

COUGH MIXTURES

Iodopropylidene glycerols: ORGANIDIN, Denver

Description.—A selective mucolytic agent for respiratory conditions, containing complex of iodopropylidene glycerols.

Indications.—Chronic bronchitis, asthma, emphysema, obstructive sinusitis; bronchiectasis; postoperative atelectasis.

Administration.—*Adults:* Organidin Solution, 20 drops 4 times a day with liquids. Organidin Tablets, 2 tablets 4 times a day with liquids. *Children:* Organidin Solution, 10 drops 4 times a day with liquids. Organidin Tablets, 1 tablet 4 times a day with liquids. As a mixture: 1 oz. Organidin Solution with 3 oz. of cough preparation.

How supplied.—Organidin Solution 50 mg. per c.c., 30-c.c. dropper bottles. Organidin Tablets 30 mg. tablet in bottles of 100.

TRIAMINICOL Syrup, Anca

Description.—Each 5 c.c. contains: Triaminic 25 mg. (phenylpropanolamine hydrochloride 12.5 mg., pheniramine maleate 6.25 mg., pyrilamine maleate 6.25 mg.), Dormethan (brand of dextromethorphan hydrobromide) 15 mg., ammonium chloride 90 mg., in a red, fruit-flavoured, non-alcoholic vehicle.

Indications.—As a decongestant and antitussive in respiratory infections, coughs, etc.

Administration.—*Adults,* 1 to 2 teaspoonfuls every 3 or 4 hours. *Children* 6 to 12 years, 1 teaspoonful every 3 or 4 hours; under 6 years, dosage in proportion.

How supplied.—Bottles of 4 and 16 fl. oz.

TRIAMINIC Tablets, Syrup, Anca

Description.—Each yellow timed-release Triaminic Tablet contains phenylpropanolamine hydrochloride 50 mg., pheniramine maleate 25 mg., pyrilamine maleate 25 mg. Half of each ingredient is released promptly and the balance in 3 to 4 hours. Each 5-c.c. teaspoonful of Triaminic Syrup contains $\frac{1}{4}$ of the total tablet content in a flavoured non-alcoholic base.

Indications.—To relieve nasal and sinus congestion in colds, nasal allergies, sinusitis, rhinitis and postnasal drip.

Administration.—Tablets: adults—one tablet, swallowed whole in the morning, mid-afternoon, and in the evening. In postnasal drip, one tablet at bedtime is often sufficient. Syrup: Adults—two teaspoonfuls every 3 to 4 hours. Children, 6 to 12 years—one teaspoonful every 3 to 4 hours; under 6 years—dosage in proportion.

How supplied.—Tablets—50's and 250's; Syrup—4 and 16 fl. oz.

MISCELLANEOUS

Warfarin sodium: WARNERIN (Pr), Warner-Chilcott

Description.—Compound of 4-hydroxy-coumarin, anticoagulant. Tablets of 5 mg. (green), 10 mg. (yellow) and 25 mg. (pink). Parenteral form, 75 mg. in sterile vial with separate 3 c.c. distilled water.

Indications.—Whenever anticoagulant therapy is indicated, as in coronary thrombosis, thrombophlebitis, thromboembolism.

Administration.—Initially, usually 50 to 75 mg. orally, intravenously or intramuscularly. For maintenance, 5 to 10 mg. daily, or every second day adjusted to patient's response. In long-term therapy 5 mg. daily normally maintains elevated prothrombin time $1\frac{1}{2}$ to 2 times normal. Prothrombin-time determinations at appropriate intervals are important. *Contraindicated* in ulceration or malignant tumours of gastro-intestinal tract, in impaired liver or kidney function, in postoperative stage of brain or spinal cord surgery, and in patients undergoing continuous tube drainage of stomach, intestine or urinary bladder.

How supplied.—Tablets, bottles of 25 and 100. Parenteral, 75-mg. vial with separate 3 c.c. ampoule distilled water.

METRECAL, Mead Johnson

Description.—A complete food, in powdered form, containing all known essential nutrients, including protein, carbohydrate and fat with added vitamins and minerals.

Indications.—As the sole source of nourishment in reducing programs of the overweight; in conjunction with low-calorie foods when more liberal calorie intake is indicated; to maintain desired weight once it is attained.

Administration.—One can ($\frac{1}{2}$ lb.) mixed with 32 oz. water makes four large glasses. Used as the total daily diet, this quantity provides 900 calories. One glassful may be taken for each meal and one at bedtime, or the total quantity may be divided into more or fewer servings throughout the day.

Cautions: If reduction in number of bowel movements occurs (as in any diet with low bulk content), a bulk laxative may be advisable.

How supplied.— $\frac{1}{2}$ -lb. cans in three flavours—plain, chocolate and butterscotch.

Isosorbide dinitrate: CARVASIN Tablets, Wyeth

Description.—Each white, scored tablet contains 10 mg. of isosorbide dinitrate.

Indications.—As a long-acting coronary vasodilator for the therapeutic and prophylactic management of angina pectoris. Its onset of action is within 15 to 30 minutes and action continues for 4 to 5 hours.

Administration.—Average dose is one tablet (10 mg.) taken half an hour before meals and at bedtime. Dosage range is from 5 mg. to 20 mg. Individualization of dosage is recommended for maximum therapeutic effect.

How supplied.—Bottles of 100 and 500.

SURGICAL Absorbable Haemostatic Cones, J & J.

Description.—An absorbable coagulant in tablet form for post-extraction use. It is prepared by a special process which converts sodium cellulose glycolic acid ether into a purified haemostatic absorbable compound—modified carboxymethyl-cellulose.

Indications.—May be used in bleeding problems following tooth removal, odontectomy, alveolectomy, or small cyst excision. Effective in cases where there is a history of bleeding, and has been used successfully with patients who are on anticoagulant therapy, although the usual supportive measures should, of course, be employed.

How supplied.—Individually packaged, sterile, 75 mg. cones, 48 to a box.

REVIEW ARTICLE

THE FREE CANCER CELL*

NORMAN C. DELARUE, B.A., M.D., M.S. (Tor.),
F.R.C.S. [C.], F.A.C.S.,† Toronto

INTRODUCTION

DURING THE year 1938-1939, the present author prepared a review of "cancer research" to that date, summarizing the information concerning carcinogenesis by hydrocarbons, the relationship of viruses to the production of cancer and the effect of cancer antibodies. He was naïve enough at that time to think that much of the experimental material would quickly find human application. Now, of course, all are aware of the difficulties in applying animal research to the problems of human cancer. Nonetheless, two decades later we stand on the brink perhaps of great therapeutic discoveries.

Sir Stanford Cade, speaking at the American College of Surgeons meeting in 1958, described one of the sessions as "an historic occasion" since it was given over to a symposium on "the free cancer cell". He felt that this established a fundamental change in our thinking, transferring attention from the pathology of the dead cell to that of the living cell. He suggested then that carcinoma should be considered a biological abnormality and not a disease represented by a tumour. He wondered whether this disease process might preferably be called "cancerization".

It might well be said that the 1950's represented the golden decade of cardiovascular surgery. Perhaps it is safe to predict that the 1960's and subsequent decades will be those dedicated to cancer eradication. Certainly this is potentially the most exciting and rewarding field in medicine today.

We are all aware of the enormity of the problem faced, but surgeons generally are beginning at last to look beyond the simple concept of repetitive emphasis on early diagnosis and total wide excision, although both of these principles will undoubtedly remain important in appropriate cases. The initial concern of the surgeon in the treatment of cancer remains the eradication of the primary tumour, but control of metastatic disease is now recognized as an integral part of attempting "cure" of the disease.

In the past attention was directed towards attacking the disease as it extended by continuity and via the lymphatic system. However, the presence of dissemination by implantation and via the venous system, although recognized, has long been neglected, despite the fact that venous metastases are the usual causes of death.

During the past 50 years several reports have been presented describing abnormal cells, thought

to be malignant, in the blood stream of cancer patients, but the identification of these cells appeared doubtful and, therefore, the reports were largely ignored until recent years. It is with the significance of these cells and the directions of study in which their discovery leads that this present report will largely deal.

A. LOCAL IMPLANTATION BY THE FREE CANCER CELL

In considering this problem of cellular implantation or vascular dissemination, the following fruitful pathways of study may be briefly summarized.

Turning first to the problem of implantation and local recurrence, washings from open wounds, from instruments, and from the surgeon's gloves in cases in which carcinoma has been resected will frequently reveal the presence of desquamated cancer cells.¹ Recently, it has been shown that both pleural and peritoneal washings demonstrate the same findings.² About one-third of pleural washings are positive for malignant cells when the operation is for bronchogenic carcinoma, with approximately 20% positive results in resectable cases and 40% in non-resectable cases. Surprisingly enough, this finding does not appear to be influenced appreciably by operative manipulation, since there were just as many positive washings before manipulation as were demonstrated after the operative manipulation.

In the case of peritoneal washings,² about 50% were positive in tumours of the stomach (31 of 59 cases) and colon (38 of 89 cases) and one-third to three-quarters of the cases respectively were positive in carcinomas of the uterus (22 of 66 cases) and ovary (28 of 36 cases).

This finding of contamination by malignant cells, and the appreciable incidence of local recurrence in neck dissection, mastectomies and colon resections have led to the search for wound irrigants capable of eradicating the cells. Various chemical substances and chemotherapeutic agents have all been studied in this search for a satisfactory agent.³ The dosage level of alkylating agents which are effective closely approaches toxic levels and for combined local and systemic use it is necessary to know exactly how much is absorbed from the wound. Therefore, although these agents may be quite satisfactory in closed cavities, such as the pleural and peritoneal spaces, in which cases a known amount is absorbed, they may be dangerous when used in the irrigation of open wounds. If no adjuvant systemic use is contemplated, then small amounts, properly diluted, can be safely used as local wound irrigants. However, if adjuvant chemotherapy is to be used, one must search for a drug with minimal systemic toxic effects. As far as wound healing is concerned, triethylene thiophosphoramide (Thio-tepa) is possibly safe because it has no vesicant action, and nitrogen mustard in proper dilution can also be safely used. Moore

*Presented to the Surgical Section, Academy of Medicine, Toronto, January 19, 1960.

†Assistant professor of surgery, University of Toronto.

reports⁴ that in a strength of 5 mg. % there is no detectable interference with wound healing in human subjects when nitrogen mustard is used in this way.

Experiments in this investigation have primarily involved the preparation of subcutaneous pouches into which tumour is inoculated and subsequently irrigated by the agent one hour after the inoculation.³ In controls approximately 89% will form a tumour; this figure falls progressively with most of the different agents studied to a level of 5% in the case of 2% monoxychlorosene (Clorpactin) and 3% when nitrogen mustard is used. It is interesting and perhaps important to record the fact that when saline, water, heparin or Terramycin was used the incidence of successful inoculation rose to 100%, with faster growth and the production of larger tumours. This is thought to be due to the fact that mechanical irrigation with these substances drives the inoculated tissue into crevices in the wound where they may readily grow.

One should also digress for a moment to note that the strength of monoxychlorosene used in this study is one which cannot be used clinically, as there is definite evidence of systemic toxicity at this dosage level in dogs.³ It is suggested that the chemical may be used in 0.5% dilution in closed cavities and that 1% dilution is safe in open wound irrigation in amounts up to 1500 c.c.³ One plan, as outlined for use in radical mastectomy,³ suggests that the wound should be irrigated every 45 minutes with 250 c.c. of 1% solution utilizing an Asepto syringe for flushing the wound, the material being left in contact for about three minutes. At the completion of the operative procedure the wound is irrigated finally with 500 c.c. of the solution and then flushed with saline. Gloves are soaked in 0.5% solution before closing the wound.

The University of Illinois Group⁵ report that in experiments similar to those described above, using the 1% dilution, the "take" increased from 6% with the 2% solution to 46%. Hence the rationale of frequent irrigation and a three-minute period of contact.

Cole⁶ has also demonstrated the intraluminal presence of viable cells which are washed away by the faecal stream passing over the surface of colorectal growths. These cells have been demonstrated in enemata and result from the washing of the cells distally by the peristaltic activity of the affected bowel. This explains the rationale of applying tapes above and below the primary tumour when undertaking colon resections with irrigation of the loop *below* the site of the anastomosis with effective cancericidal drugs (e.g., mercury bichloride).⁷ It appears probable that carcinoma never implants itself on intact epithelial surfaces, but is engrafted readily on raw surfaces, such as suture lines or bleeding hæmorrhoids.⁸

B. VASCULAR DISSEMINATION OF THE FREE CANCER CELL

In regard to the presence of malignant cells in the blood stream, these cells are usually thought to result from the direct invasion of local venous radicles, although it is apparently quite definite that they may also reach the blood stream by invasion of the lymphatics, eventually traversing the thoracic duct. Recent evaluations⁹ by means of cannulation of the thoracic duct report that 23% of the specimens studied are positive for malignant cells, and particularly in the case of lung and stomach cancers this becomes a very frequent finding, probably occurring in better than 50% of cases. These findings support, of course, the original recognition by Virchow in 1848 that the thoracic duct was important in tumour spread. In bowel lesions it is also possible for the cells to invade the inferior vena cava when periaortic nodes are involved.⁸

In assessing the results reported in studies of malignant cells in the blood stream we must remember that these cells are found in almost fortuitous fashion at the time of a momentary examination when the specimen is obtained. In all probability, were a continuous sampling of the blood stream to be feasible, one would discover that in most, if not all, instances these cells appeared regularly in the blood of patients harbouring carcinoma. The fact too that they are found in the peripheral blood¹⁰ as frequently as in local venous drainage means that the lungs and liver are ineffective barriers to tumour cells. These cells have been shown to pass through the liver and lungs in animals. Glass spheres up to 500 microns can be shown to pass through normal human lungs, whereas spheres up to 180 microns will pass through the liver of animals without difficulty.¹⁰ Cells in the antecubital vein have obviously passed through two capillary beds, those of the lungs and the arterio-venous connections. When they are found in cases of gastro-intestinal carcinoma, it means the addition of a third capillary bed in the liver. If they are capable of traversing these beds, what is to prevent them from passing through many more capillary beds as time goes on? It is interesting to record too that these cells always appear to be healthy and one seldom sees degenerating cells in the smears.¹¹

In the initial reports it was thought that cancer cells were found in the blood stream only in advanced cases but it became apparent very early that at least 15% of these positive findings occurred in cases of resectable and potentially curable cancers.¹²

At our hospital we have primarily studied lung, breast and colon cancers, specimens being taken in the preoperative period, during operative manipulation, and again in the postoperative period. Preoperatively both lung and breast cancers have positive blood findings in approximately 25% of

cases. Interestingly, cases of colon cancer are positive in 49%; this is related possibly to the trauma attendant upon normal or abnormal peristaltic activity. During the period of operative manipulation the incidence in lung and bowel cancer rose to 66% and in breast cancer to 50%. We were greatly intrigued by the finding that these cells remained in the peripheral blood stream during the postoperative period, in 58% of cases of lung cancer, 36% of breast cancers and 46% of colon cancers. We are not at the moment prepared to speculate on the significance of this finding, although it is interesting to record that the Montreal group have also shown persistence of these cells postoperatively up to nine days in 63% of their cases.¹⁰ They report also that the percentage of persistence increases in cases in which there is evidence of nodal involvement. Other groups¹³ have had some difficulty in demonstrating this persistence of cells in the blood stream postoperatively, possibly owing to the fact that a different type of case is studied.

Although it is known that blood cells survive passage through vascular filters for appreciable periods of time, it seems scarcely credible that tumour cells several times as large would continue to do so without becoming arrested somewhere during this period of free circulation. The trauma alone attendant upon such repeated passage through channels normally narrower than the cells themselves, no matter how distensible the channels may be, might be expected to produce degenerative changes if not complete destruction. In the case in which clumps or established colonies are disseminated this seems still more improbable.

Presumably in lieu of this alternative they must be spread from metastatic foci that are not detectable clinically, and it is possible therefore that their presence might indicate the extent of the disease, in which event this factor would become an important feature in prognosis.

All groups, however, have demonstrated the same increase at the time of operative manipulation. Ross, studying cancer of the lung, found that the preoperative level of 15% rose to 70% at the time of operation, although one week postoperatively he was unable to demonstrate any persisting cells.¹⁴ Roberts found that negative blood samples preoperatively became positive at the time of operation in five of seven cases studied in this way.¹⁵

C. SIGNIFICANCE OF CIRCULATING CANCER CELLS

If such cells are found so frequently in the blood stream and are quite possibly present at some time in all cases of cancer, why do we not constantly see metastatic disease? The significance of these circulating cells, therefore, needs careful assessment.

Engell¹⁶ has made the only lengthy follow-up study of these patients and has found that of those surviving five to nine years after surgical treatment,

51% had in fact tumour cells demonstrable in their blood stream at the time of operation. He holds, therefore, that these cells must have been destroyed. Morley¹⁷ has also demonstrated that tumour cells can be found in the sagittal sinus venous blood in patients with glioblastomas, although metastases never develop in this disease.

In attempting to prove that these cells are indeed "cancer cells", Taylor¹⁸ has reinjected them into a human host, failing, however, to reproduce the tumour. These cells have been injected into skin, subcutaneous fat, and muscle but admittedly the number injected is comparatively small and is associated with a large number of leukocytes capable of releasing enzymes and producing a lytic reaction which may affect the survival of the inoculated cells. It has been demonstrated¹⁹ that in mice if cells of this type are injected directly into the heart of animals of the same strain tumours are developed. Jonasson²⁰ has similarly produced "takes" on injection of these circulating cells in experimental animals. Since Moore²¹ has also found it possible to grow these cells in tissue culture, it is generally accepted that they are viable living cells which must be destroyed in some way in order to prevent them from producing recognizable disease.

In this problem the situation resembles that encountered in bacterial infections where established infection becomes apparent only when an overwhelming number of organisms are inoculated; when the organisms are extremely virulent, or when the ability of the host to mobilize the normal defence mechanisms is lost. Therefore, it would appear that the development of metastatic foci depends not only upon the nature of the cells disseminated, but also upon the reaction of the host. Let us begin then with a discussion of the nature of the dissemination.

1. The Number of Circulating Cells

In experimental inoculation the percentage of "takes" increases with the number of cells inoculated,²² particularly if clumps of cells are used.²³ The free floating cell itself may be of relatively little significance, as there is evidence that the reticulo-endothelial system can dispose of these individual cells readily. One should note in this instance the rarity of metastatic carcinoma in the spleen. Certainly Dockerty described this situation very well when he stated that for every metastatic take of blood-borne cells there are hundreds or thousands of instances in which these cells "wither on the vine".⁸

However, when groups of cells gain entrance into the lumen of a vein they set up a clotting mechanism which results in the propagation of a fibrin clot that acts as a seed bed for the malignant nidus. Subsequent dislodgment of the clot carries malignant cells to their metastatic outcome in well-established colonies.⁸ The importance of this factor is suggested by the fact that small obstructing

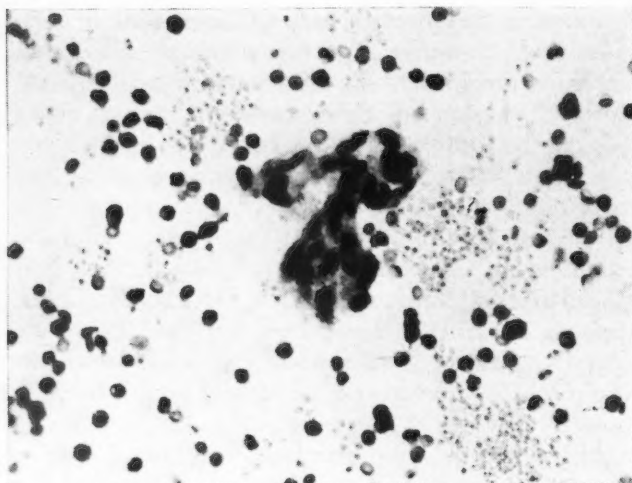


Fig. 1a.—Clump of malignant cells. Hæmatological technique.

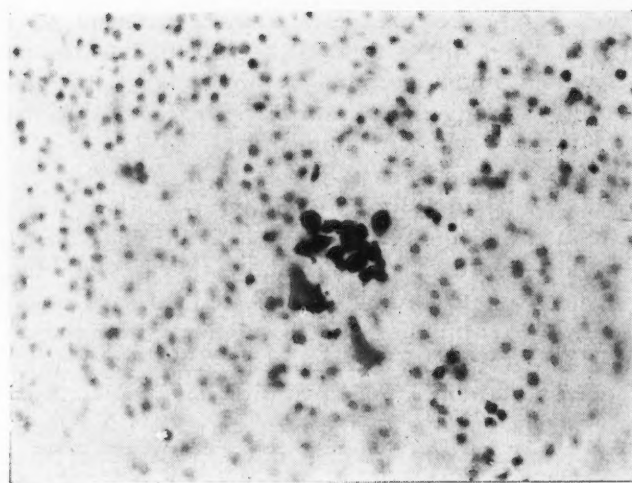


Fig. 1b.—Clump of malignant cells. Millipore filter technique.

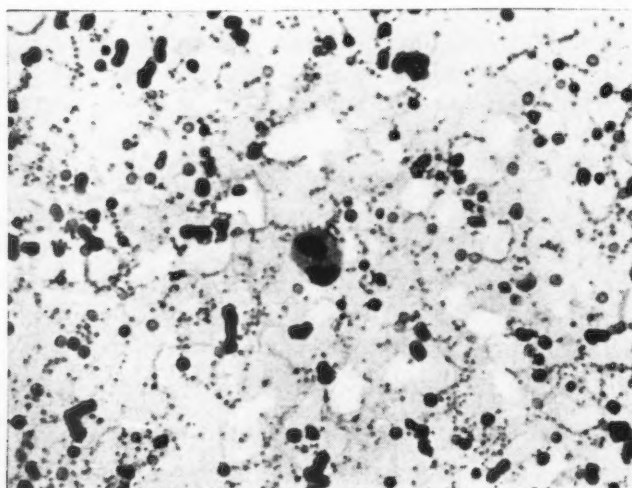


Fig. 2.—Free cancer cells.

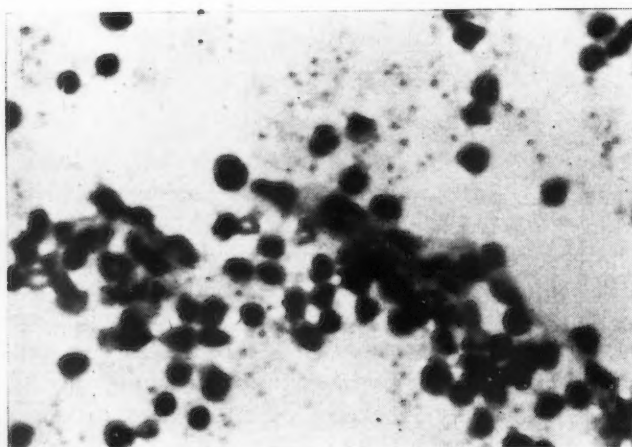


Fig. 3a.—Clump of leukocytes.

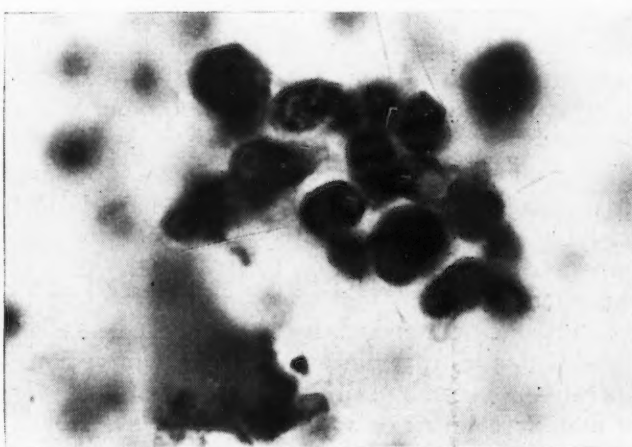


Fig. 3b.—Clump of malignant cells. Millipore filter technique.

colonic carcinomas, no more anaplastic than their more bulky silent cousins, have a much higher rate of vascular spread in producing metastatic disease, presumably as a result of the massaging effect of hyperperistaltic activity. In the examination of such resected specimens as these, if the blood vessels show carcinomatous invasion the five-year survival rate falls from 75% to 30%.²⁴ Similar findings have been reported for lung cancer by Gagnon,²⁵ who

states that all those surviving longer than two years had no evidence of blood vessel invasion in their primary lesion, whereas, with but one exception, all those dying of secondaries did have blood vessel invasion. As is now customary in pathological appraisal, he stressed the fact that the fundamental histological picture did not influence the prognosis directly. The probable displacement of major clumps of malignant cells such as these account for the rationale of early high ligation of venous drainage in resection of colonic carcinoma. As an extension of this line of thought one may also undertake the resection of large solitary metastases which appear some time after the treatment of a primary tumour or are perhaps discovered at the time of the original operation, because it may be felt that the patient has a reticulo-endothelial

system capable of handling other less gross seedlings.

2. The Biological Nature of the Circulating Cell

Although the number of cells disseminated is of obvious importance, the nature of the individual cell released may also have some fundamental bearing upon the development of metastatic dis-

ease. In the first place the local extent or stage of the disease is apparently capable of influencing the number of positive specimens obtainable on examining peripheral blood. Cole¹² found 16.7% positive in curable lesions whereas 31.1% became positive in the incurable or advanced stage of local disease. Although the local extent is probably less significant than the grade of the tumour, it is apparent too that in rectal carcinoma¹⁶ it has some bearing on the problem, since those falling into the Group A classification of Duke showed 41% to be positive for circulating cells while those in the C classification showed a 70% incidence of positive findings. However, the incidence of circulating cells seems to be more closely related to the grade of tumour, according to Engell,¹⁶ who found 34% of specimens positive in grade II, 76% positive in grade III, and 100% positive in grade IV lesions. Both the local extent of the primary lesion and the pathological grade of the cellular detail probably represent the maturity of the lesion in relation to the host, or, in other words, the biological age of the cell.

It is important to stress the fact that there is a continuing variation and selection of cells within a tumour cell population. Roberts²⁶ has reported that cell populations are not homogeneous but heterogeneous, with the different cells identifiable by their appearance, these cells living together in dynamic equilibrium and altered by changes in the environment with selective changes in the make-up of the tumour as a whole. Drug therapy of carcinoma may produce a remission which is only temporary and when the tumour reappears it is now resistant to the drug and progresses to a lethal result despite further treatment. This resistance does not appear to be due to a mutation induced by the drug, but to the presence of pre-existing variant cells. The drug therapy kills the rest of the cells but the variants survive, proliferate and produce a resistant neoplasm. Each tumour studied had one (or more) strains of stem-line cells responsible for the main growth of the tumour, and outside the stem-line there was a variable number of genetically unbalanced cells doomed to extinction in one or more cell generations.

In the main, there are two principal groups of cells classified according to chromosome count, those near the diploid number and those near the tetraploid number. Tumours with a modal diploid constitution are strain-specific as far as transplantation is concerned, whereas tumours of the tetraploid type show varying degrees of indifference to the host of other genetic constitutions. As tumours mature, biological degradation of the diploid cells occurs and tumour population is gradually replaced by the aggressive stem-line cells. Hence the statement that the stage and grade and the incidence of circulating cells are related.

Assuming this possibility on theoretical grounds before there was actual histological evidence of a

varying tumour cell population, we have in this institution for many years in the treatment of breast cancer felt that one should "nibble away" at metastatic disease rather than attempt to use all possible therapeutic gestures at once, since in the latter instance dependent cells might be completely destroyed, leaving a clear field for the proliferation of the stem-line cells and the rapid production of a virulent, aggressive and lethal tumour. We have preferred to take advantage of the competition for nutritive substances that must take place between the varying elements of the tumour population itself, thus attempting to control the proliferation of the vital cell by taking advantage of this intra-tumour competition in addition to the natural resistance of the host itself. We call this principle one of sequential therapy.

We have felt that the modal diploid cells may be sensitive to the natural mechanisms of resistance of the host and perhaps therefore incapable of setting up effective functioning metastatic disease. This thesis would explain why all the cells found in the blood stream may not be significant. Such a thesis is supported in the discussion of a Bethesda report²⁷ at the American College of Surgeons meeting in 1959, when it was mentioned that metastatic cells were more polyploid than the normal diploid cells and also by the report from Moore²⁸ that when using polyploid cells it was easier to produce metastases than when using cells of the usual diploid number.

This possibility is one of the reasons why the primary tumour should always be eradicated if possible, provided the patient does not already have evidence of actively growing and potentially lethal metastases. Despite the presence of circulating cells in the blood stream one may in this way prevent maturation of the primary tumour and eradicate the lesion while it is still composed largely of dependent cells, before their biological degradation and replacement by cells of a more virulent type. Consequently, the disseminated cells, being of modal diploid type, might be expected to fall prey to the natural resistance of the host, whereas the cells spread during later biological development of the tumour would be more aggressive and not susceptible to the forces of host resistance.

D. SIGNIFICANCE OF "HOST RESISTANCE"

In regard to the problem of the host reaction to the presence of these cells either in primary foci or when disseminated through the blood stream, it is customary to use the term "resistance" in describing this host reaction. The importance of resistance has been demonstrated by producing a diminution in the resistance by various measures. There is no recognized way at the present time in which the host resistance may be specifically improved to combat any single tumour, although steps are being made in this direction.

1. The Effect of "Stress"

The importance of resistance can be demonstrated in experiments designed to diminish the resistance. It has long been suspected that the virulence/resistance ratio was important in the establishment of metastases and that in many cases of high host resistance and low virulence of the disseminated cells these loose cells floating in the blood stream may not be clinically viable. However, if the ratio is reversed, the majority of these cells might live and be capable of setting up metastases. In one experiment²⁹ tumour was inoculated in the leg of an experimental animal and the leg subsequently amputated, with a rubber tourniquet above the lesion so that cells were not disseminated by the operative manipulation. The incidence of pulmonary metastases was much greater in animals whose legs were amputated than when amputation was not performed, and since it is fair to assume that cells are disseminated equally in both groups the operation must have lowered the resistance, permitting the survival of metastatic foci. A similar effect of stress³⁰ may be demonstrated by the increased percentage of "takes" after primary inoculation when the animal is stressed by a coeliotomy at the time of subcutaneous inoculation of the transplantable tumour. Pre-treatment with cortisone, which simulates operative stress, and pre-treatment with chemotherapy, followed by intravenous inoculation of cells, are also reported to increase the "take" of these inoculated cells.³¹

Many features are important, of course, in assessing the components of this resistance phenomenon. Nutritional factors are undoubtedly significant, since low-protein diets inhibit the development of spontaneous hepatomas and in artificially induced hepatic metastases an increase in dietary protein from 18 to 30% will more than double the "takes" from intravascular injection. However, acute starvation which affects the host resistance rather than the local depletion of protein in the tissue will also produce an increased incidence of "takes". Acute starvation, of course, produces an adrenocortical response identical with that induced by trauma, and in addition produces a diminution in the lymphocyte count which, as will be indicated, may well be of fundamental importance in the immune reaction.

Going back to the experiment in which limbs with growths from inoculated tumour were amputated, we should comment that although metastases were increased after amputation,²⁴ the animals which had their limbs amputated actually lived longer than the controls. This was because of the development of malnutrition in the host, nitrogen being utilized by the tumour at the expense of the host. In other words, a growing neoplasm continues to provide itself with the nutritional elements necessary for growth regardless of the intake of the host, who may actually be

in negative nitrogen balance while the tumour continues to grow. Surgical treatment must, therefore, be planned to balance the benefit of removing the primary tumour against the potential danger of operative dissemination.

The stress of cold³³ produces an increased susceptibility to "take" just as does operative stress, and interestingly enough propylthiouracil in dosage sufficient to induce hypothyroidism will block this stress reaction and protect against cold stress.³⁴ In hypothyroid states the stress reaction to nitrogen mustard or coeliotomy is also blocked, and therefore nitrogen mustard utilized in these states will produce a marked reduction in "takes" of inoculated cells without adversely affecting the resistance of the host.

2. The Effect of the Lympho-reticulo-endothelial System

Cytotoxic drugs are known to damage the haemopoietic and lympho-reticulo-endothelial systems and, as noted above, pre-treatment with chemotherapy may increase the incidence of subsequent "takes" on tumour inoculation. There is other evidence to suggest that the lympho-reticulo-endothelial system is important in the development of resistance in a patient to the presence of cancer.

When rats are inoculated with suitable tumour cells, only 25% will survive, whereas if the inoculum of tumour cells is given with lymphocytes or serum from immune rats, 75% of these animals will survive.³⁵ It has been noted in addition that the lymphocytes of the immune rats retain this anti-cancer property when treated with nitrogen mustard or triethylene thiophosphoramide (Thio-tepa).

This relationship can also be demonstrated in spontaneously developing tumours, such as the malignant melanoma of hamsters.³⁶ Minced tumours are injected into rats as an heterologous host to provide immune serum and also immune splenic extract which is greater in potency and duration of effect than the serum. If the tumour plus the immunized serum or spleen extract is then injected into hamsters, a marked diminution is found in the growth of the tumour.

The immune reaction can be transplanted by living cells and this effect is thought to be directly cytotoxic rather than an antibody effect as in the serum. In testing this tumour-inhibiting effect of homologous living cells³⁷ Wistar rats, which survived the growth and regression of lymphosarcoma transplants, proved to be immune to subsequent transplants. Cell suspensions of varying tissues from these tumour-immune animals were assessed for anti-tumour effect in protection against the lethal effect of intraperitoneal implants in young rats. It was discovered that both living lymphocytes and living testicle cells provided effective protection, although the dosage was important, having to be of the order of 500 lymphocytes for a single tumour cell. This is, of course, related to the necessity for

the injection of large numbers of cells if metastatic deposits are to be produced.

It has become apparent that human cancer tissue exhibits the same biological features as normal tissue and, therefore, it is worth while reviewing the important features of tissue transplantation briefly. They may be summarized as follows:³⁸

1. Transplants are rejected by healthy homologous recipients.
2. Rejection of transplant induces an enhanced ability to reject subsequent transplants of similar type.
3. Rejection is not associated with demonstrable amounts of antibodies.
4. Transplants survive in subjects with agammaglobulinaemia.
5. Rejection and subsequent accelerated response appear to be dependent upon circulating lymphocytes.
6. Regional lymph nodes respond to homologous transplantation by lymphoid hyperplasia (large lymphoid cells in the medulla).
7. Rejection is associated with the appearance of lymphoid infiltrates in the region of the degenerating tissue graft.

Medewar³⁹ suggests that lymphocytes are concerned with the recognition of "foreign" (i.e. antigenic) materials and that their nucleoproteins are in equilibrium with those of the tissue cells, which may be called "self" proteins. If the young fetus is inoculated with foreign protein, the host is unable to recognize the inoculation of this protein as foreign in later life.

Hirsch⁴⁰ has made the statement that tumour cells originate in the body by mutation or from other causes *all the time* but that those most different from host tissue are destroyed by the body's immunological reaction, and only those *very similar* to host tissue have a chance to develop into a tumour because immune response is very weak. Grade IV lesions might well therefore be made up of biologically old, potentially virulent cells. One should note in this regard that lymphoid infiltrates are not commonly seen in the majority of cancer cases and when lymphoid infiltration (which visualizes antigenic changes) accompanies the invading tumour cells the clinical course is prolonged. There is a question as to whether these changes represent partial loss of "identity" protein or the presence of a high degree of antigenicity. Certainly the finding of reactive nodes at the time of surgery in "early cases" and the discovery of degenerating nodes at post-mortem examination in "late cases" suggests the importance of this lympho-reticulo-endothelial reaction. Because this system is sensitive to chemotherapeutic agents, their use in early cases may do more harm than good by producing a diminution in the essential resistance of the host.

E. SUMMARY OF CLINICAL APPLICATION OF DATA REGARDING CELLULAR DISSEMINATION: HOST RESISTANCE RATIO

I. Measures to Prevent the Adverse Effect of Surgical Treatment.

1. Early treatment before maturation of the primary neoplasm.
2. Limitation of wound implantation by gentle surgical technique and the use of effective wound irrigants.
3. Limitation of vascular dissemination, again by gentle surgical technique and early ligation of venous drainage channels.
4. Avoidance of unnecessary stimuli, physical, emotional and biochemical, which might aggravate the effect of the operative stress in diminishing the resistance of the patient.

II. Measures Designed to Limit the Adverse Effect of the Disseminated or Free Cancer Cell.

1. *Use of preoperative radiotherapy.*—Since the reason for failure in surgical treatment of cancer is primarily the dissemination of viable cancer cells either into the circulation to produce metastases or locally to produce recurrent disease, attempts to alter the ability of these cells to implant and grow may improve the results. Experimentally⁴¹ this has been approached by testing the effect of preoperative radiotherapy followed by intra-vascular injections of the treated cells and subsequent estimation of the number of lung metastases produced. A dosage of 150 roentgen units (r) reduces the incidence up to 40%; 715 r, up to 70%; and 2000 r, up to 80-100%. This demonstrates that amounts of irradiation which are too small to alter noticeably the growth of primary tumours do significantly alter the ability of its cells to implant when artificially disseminated into the circulation, and perhaps small doses of this type *do* have a place in therapy. In the past radiotherapists have preferred to refuse treatment or else deliver a full cancericidal dose of radiotherapy, fearing that small doses actually stimulated growth of the lesion. Certainly when using immune rats which are subsequently challenged by additional inoculations of cancer cells, radiotherapy alone³⁵ appears to have no effect in diminishing the resistance to such implantations.

We have attempted to evaluate the importance of preoperative radiotherapy in the treatment of advanced primary mammary carcinoma. Certainly the incidence of locally recurrent disease appears to have been beneficially affected by this additional measure in management, but it has been difficult to decide whether the survival rate is significantly affected by the addition of such a major form of therapy; on the basis of experimental results one would now wonder whether the dosage level of radiotherapy had been excessive, considering the aims that it is hoped to achieve.

2. *Use of adjuvant chemotherapy.*—The original observation that protection against the development of hepatic metastases resulting from intra-portal injection of tumour cells could be achieved by the adjuvant exhibition of chemotherapeutic agents⁴² has led to a consideration of the value of adjuvant chemotherapy in clinical conditions. Since pre-treatment with chemotherapy³¹ followed by intravenous inoculation may increase the number of "takes" in experimental animals and because nitrogen mustard therapy for established tumours which are relatively insensitive to the therapy increases the number of circulating cancer cells in the blood stream,⁴³ one may be concerned about the dangers of adjuvant chemotherapy of this type. This is particularly important when it has been established that samples of blood, taken from these animals in which the number of circulating cells has been increased, and injected into other animals pre-treated with cortisone, will produce "takes" of the injected cells. This means that these liberated tumour cells are viable. One must therefore attempt to pick out cases of sensitive tumours so that the beneficial effect of the adjuvant chemotherapy will be greater than the toxic effect on the normal cells of the host, which may diminish resistance. Presumably the diminished resistance is due to the cytotoxic effect on the lympho-reticulo-endothelial system. It has been noted⁴⁴ that chemotherapy applied in this manner occasionally results in a rapid spread of the tumour under treatment, and this has been attributed to just such an adverse effect on host "resistance".

III. Measures Designed to Improve the Host "Resistance":

(a) *Production of active immunity.*—The ultimate aim, of course, is to produce active immunity and this may be attempted by developing autogenous vaccines for use in cancer patients. This concept is based on the fact that some part of the tumour is probably antigenically different from the host and that the host is therefore capable of recognizing this difference. However, it is difficult in these instances to obtain the necessary five grams of relatively pure tumour to make the cell suspension which appears to be best for injection.⁴⁵ Nonetheless, in gynaecological cancer some benefit was demonstrated in the treatment of squamous carcinoma, which had never been affected previously by chemotherapeutic agents. Interestingly enough, some patients had tumours which became more sensitive to ionizing radiation under the influence of this vaccine; this suggests the possible value of a combined attack upon the problem.

(b) *Transfer of passive immunity.*—Since little of positive value to date has resulted from efforts to produce active immunity, it is permissible to investigate the more limited goal of using the principle of transfer of passive immunity. This is usually performed by using a heterologous host,

and Buinauskas⁴⁶ has chosen the sheep since it produces a large amount of antibodies. In this heterologous host antibodies are developed to both the cancer cell and the normal tissue cells which are injected with it, and therefore the serum obtained must subsequently be treated with normal cells in order to remove the anti-normal cell antibody, leaving a fraction which contains only antibodies of anti-cancer cell type. Subsequent injection of these antibodies into the human host has on occasion produced regression of the symptoms and signs of metastatic disease. Gordon Murray⁴⁷ reports similar experiments in attempting to transfer passive immunity, using the horse as the heterologous host, in which an immune reaction is stimulated. This is an important and encouraging concept and warrants further study.

F. CONCLUDING COMMENTS

There is no field of surgical investigation or treatment which has more to offer at the present time. It may possibly be necessary to spend less time working with mice and more time working on humans who have tumours. In view of the difficulty in attempting to apply the information obtained from experimental animals to the effective management of human cancer the time has arrived for spontaneous tumours to be studied rather than the long-transplanted tumours, the tumours derived from tissue cultures or the carcinogen-induced tumours.

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GENERAL PRACTICE

LES RELATIONS DE L'OMNIPRATICIEN ET DU SPÉCIALISTE

Texte de l'allocution prononcée par le docteur Paul David, Directeur de l'Institut de Cardiologie de Montréal, à l'assemblée générale du 29 février, lors du 41ème congrès annuel du Collège de Médecine Générale du Canada.

Une Médecine n'est grande et belle que par la grandeur et la compétence de ses médecins et particulièrement le médecin de famille qui constitue présentement et pour toujours, nous le souhaitons, l'unité fondamentale. Dans certains milieux, on se plaît à opposer le médecin de famille

et le spécialiste ou le médecin d'hôpital. Cette opposition m'a toujours paru ridicule et elle repose sur des concepts qui frisent l'aberration mentale. Il me semble utile non pas de défendre le spécialiste que je suis, mais d'essayer de vous exposer les relations qui me paraîtraient idéales entre le spécialiste et le médecin praticien.

En premier lieu, l'un et l'autre, s'ils pratiquent essentiellement une médecine honnête ont une valeur égale et un mérite égal. Il n'existe pas d'aristocratie en médecine. Il n'y a pas de classe. Le spécialiste n'est pas un seigneur et le praticien un vassal. Un médecin de famille compétent, honnête, consciencieux, laborieux et dévoué a le juste droit de se sentir parfaitement à l'aise parce qu'il est l'égal de tout spécialiste qui possède ces mêmes qualités. Un complexe d'infériorité n'a pas plus sa place chez l'un, qu'un complexe de supériorité chez l'autre. Les différences qui existent sont des différences humaines, intellectuelles, morales et sentimentales. Ce sont des différences individuelles qui font que, des millions d'hommes peuplent la terre, on n'en trouve pas deux qui soient identiquement et intégralement semblables.

En second lieu, la médecine étant essentiellement une école de modestie, l'orgueil représente pour sa pratique le vice intellectuel ou moral le plus dangereux. Pour bien se comprendre lui-même et bien s'entendre avec ses confrères, le médecin doit chaque fois qu'il prend une décision médicale mesurer ses limites à l'échelle de la responsabilité de ses gestes vis-à-vis de la vie humaine. Cette responsabilité nous la sentons dans toute sa plénitude quand le malade est notre père, notre mère, notre femme, notre enfant ou un être qui nous est cher.

Quand nous embrassons du regard l'ensemble des connaissances médicales, il est bon de méditer sur le peu que chacun d'entre nous peut prétendre connaître. Les progrès médicaux s'écrivent dans des milliers de périodiques qu'aucun médecin n'a le temps de lire et même s'il l'avait son cerveau serait impuissant et incapable de saisir et de comprendre l'immense "casse-tête" que constitue la Médecine devenue une science où s'amalgame tout le savoir humain. Ces progrès sont la raison obligatoire de la spécialisation. Chaque spécialité a rétréci pour le médecin qui la pratique le territoire de ses connaissances. Et le spécialiste pourra suivre les progrès de sa spécialité jusqu'au jour où ces progrès conduiront encore à une nouvelle sous-spécialité. Ne pas admettre la spécialité en Médecine, serait retourner un siècle en arrière et quel est celui d'entre nous qui accepterait une ordonnance de 1860? Ne pas se servir de la spécialité, c'est admettre connaître toute la médecine. C'est le péché d'orgueil dont je parlais tout à l'heure.

La spécialisation n'est pas sans danger pour celui qui en viendrait à une optique ou trop simple ou trop complexe. A ce sujet, l'Abbé Pierre¹ a écrit: "La complexité des connaissances contraint l'homme moderne à se spécialiser dans des subdivisions de plus en plus exiguës d'objets de connaissance... Nous sommes en présence d'une désintégration de l'homme par excès de raffinement de la connaissance."

Le Professeur Jean Lenègre,² dans son discours d'ouverture du III^e Congrès Mondial de Cardiologie disait: "La spécialisation représente pour la médecine d'aujourd'hui, et plus encore pour celle de demain, une difficulté qu'il faudra surmonter si on veut dénier toute vérité à la boutade qui dit que le spécialiste sait tout sur rien et le généraliste ne sait rien sur tout".

En troisième lieu, et en contrepoids à l'orgueil vient s'encadrer *l'honnêteté intellectuelle et morale*. Je préfère et de beaucoup un médecin peu savant mais strictement honnête à un savant malhonnête. L'honnêteté intellectuelle consiste essentiellement à savoir s'arrêter devant l'obstacle qu'une situation concrète pose à notre savoir, c'est reconnaître en somme ses limites et avouer son ignorance devant une situation intelligemment étudiée. Dans le concret, ceci équivaut à délimiter sur les seules bases de la raison les problèmes que notre connaissance nous permet d'affronter, de ceux qui à un moment ou un autre nous dépassent.

L'honnêteté morale consiste ensuite à rechercher pour chaque problème le moyen qui nous paraît le plus susceptible de la solutionner. Je n'insisterai pas sur les aspects positifs et négatifs de cette honnêteté qui devrait en toute circonstance être la base fondamentale de notre conduite médicale. Dans "L'Homme, cet Inconnu," Alexis Carrel³ a écrit: "Le sens moral est plus important que l'intelligence. Quand il disparaît d'une nation, toute la structure sociale commence à s'ébranler".

En quatrième lieu, j'aimerais signaler que la confiance indispensable qui doit exister entre patient et médecin doit aussi se retrouver entre praticien et spécialiste. Confiance qui dicte au praticien le choix du spécialiste avant que le patient ne suggère telle personnalité, confiance qui devrait créer entre le médecin de famille et le spécialiste un climat favorable aux suggestions et à des essais thérapeutiques scrupuleusement discutés.

En cinquième lieu, je considère que le médecin spécialiste doit essentiellement demeurer un consultant, dans le sens strict du mot. Si le médecin de famille a un réel devoir de consulter un confrère spécialiste lorsque la situation d'un malade le motive, le médecin spécialiste a par contre l'obligation de retourner au médecin de famille le malade référé. Nous sommes heureux d'examiner des malades à domicile en compagnie du médecin traitant et lorsqu'un malade a été hospitalisé, nous écrivons un long résumé de nos observations cliniques et de notre thérapeutique. Nous préférons, et de beaucoup, recevoir des malades référés que des malades qui se réfèrent eux-mêmes souvent en cachette ou sans l'approbation du médecin traitant. Il faut une bonne dose de naïveté pour ne pas saisir rapidement la différence lorsqu'on interroge le malade. Le moment de la consultation n'est pas indifférent. Si j'accepte d'assez bonne grâce la consultation sociale, souvent inutile pour le malade et le médecin mais réconfortante pour la conscience familiale collective, j'ai horreur de ces consultations de dernière heure, essentiellement dictées par un scrupule terminal du médecin coïncidant avec les derniers souffles du malade.

Enfin, nous pensons que s'il est logique qu'un rapport de consultation ou d'hospitalisation soit

envoyé au médecin traitant, il est également souhaitable que le motif de consultation ou d'hospitalisation nous soit indiqué par quelques lignes qui nous permettraient de mieux saisir les buts immédiats ou lointains qui motivent notre intervention. Il ne serait peut-être pas inutile de nous indiquer brièvement la situation matérielle du malade afin de régler nos honoraires en conséquence.

Je ne m'étendrai pas sur des qualités pourtant essentielles telles la discrétion, la courtoisie, la bienveillance et même l'indulgence, la franchise et la loyauté.

Je suis persuadé qu'en méditant tant soit peu ces réflexions, on comprendra pourquoi je n'ai jamais vu de différences essentielles entre Praticien et Spécialiste. Notre premier devoir est de vous servir, le vôtre de servir votre malade et ensemble nous sommes essentiellement des confrères au service de l'humanité souffrante.

C'est précisément cette idéologie que nous essayons, avec toutes ses humaines imperfections, d'appliquer entre nous, vis-à-vis de nos confrères de pratique générale et des malades qui nous sont référés ou qui nous consultent spontanément.

Mais, malgré tous nos efforts, nous ne prétendons pas être à l'abri de l'erreur et de l'échec. Malgré les lectures, l'expérience, une instrumentation importante, des problèmes resteront sans solutions. Nous avons suivi des malades qui ont gardé le secret médical de leur mort malgré une nécropsie attentive et soignée.

Ce sont précisément ces échecs qui doivent contribuer à nous rendre humbles en dépit de nos diplômes et peut-être même de notre réputation. Ce sont ces échecs qui doivent nous stimuler à travailler davantage, à étudier plus souvent et plus longuement. Nous posons des diagnostics qui contentent notre esprit et classifient les malades; si les erreurs grossières sont rares, il faut suivre un malade jusqu'à l'examen anatomique pour se rendre compte du nombre de faits et de détails qui nous ont échappé. Même les diagnostics autrefois simples sont devenus compliqués lorsqu'ils ont été sanctionnés par des contrôles plus rigoureux ou des responsabilités plus sérieuses. La sténose mitrale qui remet en question toute l'interprétation du souffle systolique de pointe me semble un exemple, particulièrement typique. Malgré un bon millier de sténoses mitrales que nous avons maintenant examinées, dans combien de cas encore conservons-nous une hésitation envers la décision d'un acte chirurgical. Le problème n'est plus d'opérer une sténose mitrale, il est essentiellement de ne pas opérer une insuffisance mitrale prédominante.

La fièvre du matérialisme moderne ne doit pas nous faire oublier le but premier de la Médecine: servir le souffrant. "L'homme n'est véritablement lui-même, a dit l'Abbé Pierre, qu'à partir du moment où il a cherché à savoir ce qu'était l'essentiel dans cette existence qu'il n'a pas voulue et où, soudain, il s'est un jour découvert". Médecins, avons-nous à nous demander ce qu'est l'essentiel? Pour Carrel, en 1934 déjà, "L'Homme Moderne s'était affaissé dans l'indifférence à tout, excepté à l'argent". Jugement cruel d'un homme pourtant lucide. Si le matérialisme a envahi nos cœurs, si

notre première préoccupation est d'amasser des biens matériels, sous le couvert d'un hypocrite dévouement ou d'une habile science, ne nous étonnons pas si, un jour, on nivelles nos aspirations matérielles dans les cadres rigides d'un fonctionnarisme gouvernemental. Si, au contraire, nous croyons avec sincérité que la médecine n'est pas un "métier" mais une "vocation", la route de l'avenir demeure belle et large, malgré les difficultés inhérentes à toute montée spirituelle. Nous accepterons de grand cœur un programme d'hospitalisation que réclame avec force et droit le malade de cette Province, mais nous lutterons contre toute atteinte à la *liberté* professionnelle. Cette liberté, nous la conservons en autant qu'on nous jugera digne d'elle. Nous perdons nos prérogatives si jamais, la majorité du corps médical acceptait de se servir de la médecine comme d'un tremplin d'enrichissement. Méfions-nous de la vie trop facile qui endort la conscience et scandalise l'entourage. Donnons aux jeunes qui nous succéderont l'exemple d'une suffisance matérielle, d'accord, mais surtout l'exemple d'une vie riche de dévouement et de sacrifices. La jeunesse d'aujourd'hui cherche désespérément la vérité dans ce siècle qui confond toutes les valeurs en le réduisant en définitive à un dénominateur commun: l'argent.

Sous cette incidence, nous avons tous, spécialiste, scientifique ou généraliste une même et seule responsabilité: "sauvegarder la valeur intrinsèque de la vocation médicale". Tout le reste est puéril ou faux.

Je termine par une citation d'Ignacio Chavez, Directeur de l'Institut de Cardiologie de Mexico⁴ qui dans un écrit remarquable a déclaré: "Il n'existe pas de pire sorte de mutilation spirituelle, chez un médecin, que l'absence de culture humaniste. Celui qui en manque pourra être un grand technicien dans son métier, il pourra être un savant dans sa science mais pour le reste, il ne sera jamais qu'un barbare privé de ce que donne la compréhension humaine et de ce qui détermine les valeurs du monde normal. Humanisme veut dire culture, compréhension de l'homme dans ses aspirations et ses misères; appréciation de ce qui est bon, de ce qui est beau et de ce qui est juste dans la vie; détermination des normes qui régissent notre monde intérieur; désir de perfection qui nous pousse à accorder la vie à la pensée". De sorte qu'en définitive le médecin est essentiellement "un homme qui se penche sur un autre homme dans un désir d'aide, offrant ce qu'il a, un peu de science et beaucoup de compréhension et de sympathie".

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MEDICAL MEETINGS

CONFERENCE ON THE NEWER DIURETICS IN HYPERTENSION

The plethora of diuretic and antihypertensive agents now available to the doctor is a source of some confusion, and this confusion was not completely clarified at the two-day conference in New York, May 6 and 7, on New Diuretics and Hypertensive Agents, convened by the New York Academy of Sciences. At this conference most of the speakers came from the United States, but there was one notable contributor from Canada, Dr. Jacques Genest of Montreal.

Dr. Genest's contribution was a careful and detailed study of the use of the newer diuretics in a series of 13 patients with nephrotic syndromes. He pointed out the absolute necessity of obtaining knowledge of the underlying lesion in such cases before treating them. He particularly stressed the value of percutaneous renal biopsy in elucidating diagnosis. Use of biopsy would prevent such therapeutic mistakes as giving steroids in cases of nephrosis due to amyloidosis, renal vein thrombosis, or constrictive pericarditis. The drugs he had particularly studied in these cases were the thiazide group and the new diuretic chlorthalidone (Hygroton). The combined effects of a thiazide and spiro lactone proved good in a case of diabetic nephrosis, and in another case refractory to spiro lactone a marked diuresis of sodium and loss of oedema have been produced by combination of chlorthalidone with spiro lactone. Dr. Genest discussed in detail the use of corticosteroids in these cases, pointing out that much improvement could be obtained, particularly with larger doses, but wondering whether the enthusiasm for prolonged and intensive corticosteroid therapy in all cases was warranted, in view of the severe reactions. He saw no need for such intensive therapy since the advent of the newer diuretics. His studies indicated that they effectively relieved the oedema.

Many of the speakers stressed the value of the newer diuretics in treatment of hypertension, going so far as to say that they had a specific antihypertensive effect, and contrasting favourably the well-being of the patient on these drugs with the previous misery of life on ganglion-blocking agents alone. The diuretic agents which attracted the most attention both in the removal of oedema and in combating of hypertension included the thiazide group such as chlorothiazide, hydrochlorothiazide and congeners, the new phthalimidine known as chlorthalidone, and the aldosterone antagonists such as spironolactone (Aldactone). Many speakers praised a combination of these drugs, including spironolactone.

Speakers also pointed out the very difficult problems involved in evaluating the action of a diuretic, because of the two variables involved—the drug itself and the patient whose condition was changing all the time. Nevertheless, even though the potency of the newer drugs might be questioned in relation to that of the older mercurials, there was no doubt about the great convenience of administration of the new drugs which could be given orally, which were cheaper, and which were more acceptable to the patient. The drug with the longest action was chlorthalidone, which could be given three times a week successfully. One speaker listed four orders of potency of the new drugs, putting in the first group the following three drugs: benzhydro-

flumethiazide, trichlormethiazide, and chlorthalidone. Another contributor mentioned that spiro lactones reversed all the actions of aldosterone, and were the only diuretics so to do. Nevertheless it was clear that very little was really known about the mechanism of action of most of these newer drugs. It was also clear that the role of aldosterone itself both in oedema and in hypertension was not wholly clarified. Moreover, giving adrenal cortical hormones might cause the body to produce compounds antagonistic in turn to it.

A panel discussion which wound the conference up produced a great measure of disagreement among the participants. One wanted to treat all patients whose blood pressure was frequently above 150/90 mm. Hg, while another objected to this stereotyped approach. The order of treatment suggested by one speaker began with a newer diuretic; if this was ineffective, another specific hypertensive agent could be added, and if this combination was ineffective, surgery could be followed by prolonged drug therapy. It seemed that there was evidence to show that surgical sympathectomy did prolong the life of these patients, but there was as yet no definite evidence that drug therapy did so. One participant produced a useful analogy with diabetes, pointing out that this condition had been treated with insulin for years without wiping out the disease or abolishing the complications. There seems little doubt that we are prolonging life in the cases of severe hypertension, but the situation in milder cases is not too clear. All the speakers in panel discussion agreed that one should start treatment of the milder cases with a modern diuretic, though they were later accused by the conference chairman of attacking the problem of hypertension peripherally without getting to the nub of it.

Among the newer antihypertensive agents discussed were guanethidine, bretylium tosylate, which unfortunately soon produced tolerance, and the enzyme-inhibiting agents such as the inhibitors of monoamine oxidase and decarboxylase. These, however, are still in the experimental stage.

S. S. B. GILDER

Association Notes

RELIGIOUS SERVICE AT THE 93rd ANNUAL MEETING

St. George's-in-the-Pines, a small, stone Anglican church, steeped in pioneer history, has been chosen for devotions for those attending the Annual Meeting in Banff, June 13-17. Rev. George Hollywood, M.A., will take the service at 11 a.m. on Sunday, June 12. Members of the executive of the Canadian Medical Association will read the lessons.

The first Church of England service in Banff goes back to 1885 and took place in a log building on Lynx Street behind the present King Edward Hotel. The cornerstone of the present church was laid in 1889 by Lady Stanley of Preston, wife of the Governor-General. King George VI and Queen Elizabeth attended a private service there in May 1939. At that time, this was the only Church of England in the western hemisphere in which a reigning British Monarch had worshipped. Two solid silver candlesticks donated by them stand on the altar.

Plans for the Sunday service have been made by the Federation of Medical Women of Canada of which Dr. Jessie McGeachy of Saskatoon is the president. Dr. Charlotte Dafoe of Edmonton is local convener. Both will attend.

The Federation was formed in 1924 and is affiliated with the Medical Women's International Association. Dr. Margaret Collins of Edmonton will be attending a council meeting of the International Association in Baden Baden, Germany, in September. Canadian membership totals about 200; this represents about one-fourth of the women doctors in Canada.

On Monday, June 13, the Federation will hold its annual meeting at the Arrow Motor Hotel in Banff. This will take the form of a supper, followed by a business meeting. All women doctors are invited to attend, whether members of the Federation or not.

LADIES' PROGRAM

"Big Red Walkin' Hood," written by Peggy Miller of CJCA, Edmonton, will be produced, directed and narrated by her at the luncheon on Wednesday, June 15, being arranged for the doctors' wives attending the annual meeting in Banff.

Edmonton wives, who hope to pass incognito in their daring costumes, will form the cast. Of their share in this hilarious skit, they are unprofessionally reticent. But when Peggy Miller's name comes up, that is a different matter.

"She should have an honorary medical degree," said Hope Thomson, who played the part of Big Red in the Edmonton production last fall. "While she has no connection with the medical profession," Mrs. Thomson continued, "she will write, direct and frequently act in any entertainment to help local medical group needs." Radio station CJCA is also most generous in giving Peggy time off from her busy radio schedule to assist medical wives in the entertainment field.

The cast includes five principals, eight live puppets and the narrator, with able assistance from piano, drums and fiddle.

Tangible reminders of the mountains will be carried away by two doctors' wives attending the 93rd annual meeting when two original paintings are presented following a lucky draw at the luncheon on Wednesday, June 15, in the Banff Springs Hotel. From these pictures obtained by the Women's Committee, silk screens are being made and will form the cover for the program of convention events. So while only two may win the larger paintings, each woman attending will have a small silk screen print of the originals.

Janet Middleton, A.S.A., C.P.E., noted western artist, has been commissioned for the work and has depicted Peyto Lake in the Bow Valley and a mountain scene from Banff. Born in Vernon, B.C., Miss Middleton has received her training in Western Canada and is a member of the Society of Western Artists, San Francisco. She has been a member of the faculty of the Banff School of Fine Arts since 1948. Among recent honours she received a bronze medal in sculpture from the Vancouver Art Gallery and completed a commissioned mural for the C.N.I.B. building in Edmonton. In private life she is Mrs. J. M. Churchill of Calgary.

LETTER TO THE EDITOR

A WIDER CANADIAN MEDICAL OUTLOOK

To the Editor:

I have just returned from a three-month tour through the islands of the West Indies Federation and some of the territories in West, Central and East Africa which are or have been British. I met only one other Canadian doctor working in these developing countries, but a very large number from Britain, various European countries, and the United States. This is one of several reasons for concluding that Canada and Canadians lack interest in the problems of the emerging tropical countries.

To the West Indian or the African, Canada seems to have all the virtues, combining British stability and fairness with North American energy and initiative. Canada led the way from colony to independent dominion, and has the great prestige of never having been a colonizing or exploiting country. The new countries look to Canada for disinterested help and encouragement which they would not so readily welcome from elsewhere. So far this hope is largely unfulfilled, and, since Canada is not a poor country, one must lay the blame on lack of interest, or lack of a sense of adventure, or just plain smug parochialism.

Dr. Thompson's article on Canadian medical education in your Journal of April 2 tells us that each year in Canada there are about 860 graduates from 12 medical schools. By contrast, Nigeria, with twice Canada's population, has only between seven and eight hundred doctors in the whole country, and has one medical school which is just beginning to graduate classes of 20 to 30 a year. Is there any valid reason why some Canadian graduates should not work, even for a few years, in such places? There is plenty to be done: in mission hospitals, in government services, in the teaching hospitals. Some might even consider a wealth of experience to be some compensation for smaller financial rewards than Canada offers.

Dr. Struthers' paper on paediatric education has the distinction of being the only contribution to your medical education issue which refers in any way to the problems of other countries or to the possibility of Canadian doctors helping with them. He is perfectly right in his view that the rather precious North American postgraduate training in paediatrics is impractical for those who are to practise in the tropics. But he goes on to suggest that the "basic physician" in the tropical countries should concentrate at present on problems of prevention, public health, and health education, and that the locally trained doctor—in paediatrics at least—"should be group-oriented rather than individual-oriented". I disagree with this, because the best way to influence the group is through the individual. Again consider Nigeria. There, almost half the children die before the age of five. Most of the deaths are due to malaria, smallpox, measles, tuberculosis or malnutrition. Four of these are preventable—by vaccination, BCG, malaria prophylaxis, and education in proper diet. But purely preventive measures fail, because the unsophisticated African mother, like many others, takes her child to the doctor when it is sick, and not when it is well. If the child is treated when it is ill, then comes the chance for immunization and for

education of the mother. And mothers whose children have been treated and who have learned in this way are the best possible influence in their communities—better than any public health "authorities". It follows that effective prevention of disease in these communities must develop together with hospital and outpatient paediatric services.

This is where Canada should come in. Doctors interested in paediatrics are needed *now*—not to plan programs for others to carry out, but to treat sick children and to spread the gospel of health. Not, as Dr. Struthers suggests, "the provision for periods of one or two years of men who have been trained as teachers or investigators, *presumably at the resident level*, who *might* make their teaching abilities available to future medical schools which *might* be established in such areas of economic deprivation (my italics). No. Able young doctors are needed who will pitch in and work, and stick at the job long enough to learn to know these communities and their problems. Maybe some of them would gain the experience to become teachers in the medical schools which are or will be established in the developing countries.

Dr. Struthers' censure of Canadian postgraduate training in paediatrics could apply equally to obstetrics and gynaecology. Canadian obstetricians must undergo a long and expensive postgraduate training, but as specialists they spend a great deal of their time doing normal obstetrics which could be done equally well by competent general practitioners or by well-trained nurse-midwives. This is partly, but not entirely, the result of Canadian social tradition. Young obstetricians and gynaecologists in Canada might also consider giving service and gaining experience abroad. The (only) consultant gynaecologist in Northern Nigeria repaired 130 vesico-vaginal fistulae last year. Would a share in this sort of experience not be more attractive than a resident post in which even the repair of an episiotomy is a rare privilege?

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THE LONDON LETTER

(From our own correspondent)

INDUSTRIAL RHEUMATISM UNIT

In its recently published annual report for 1959, the Empire Rheumatism Council announces that it has decided to establish a special unit to make a comprehensive study of the social and economic effects of rheumatic diseases in British industry. The unit will be under the direction of Dr. J. J. R. Duthie of the University of Edinburgh. In making this announcement it is pointed out that among the employed population of Great Britain more than 730,000 persons claim sickness benefit by reason of rheumatism each year, leading to a loss of more than 27 million working days. The study of the geographical distribution of rheumatism has shown that over 80% of cases are located in industrial areas, providing a strong indication that occupational influence may be of greater importance than climatic variations.

MEDICAL ANONYMITY

At long last the British Medical Association has given way on the subject of anonymity in broadcasting. According to a "Report on advertising and the medical profession", published as an appendix to the supplementary annual report of the Council for 1959-60, "the policy of anonymity in all circumstances is no longer tenable and there is no objection to the announcement of a doctor's name" provided this conforms to certain principles. These principles are laid down as follows: "When the objective of publicity for a doctor or a group of doctors is apparent, paramount, and justifiable (a) in the interests of the general public; or (b) in the interests of the medical profession; or (c) as an essential part of providing authoritative information when necessary for the general public". It is allowed that, "when the circumstances of the broadcast specifically require it, mention may be made of the specialty, professorial chair, or office held, but not otherwise of medical appointments held". On the other hand, "a doctor engaged to give a series of talks or appearances is advised to remain anonymous lest the frequency of mention of his name should be held to be unethical" by the General Medical Council.

TOO MANY HOSPITALS?

Amid all the outcry about the lack of new hospitals there is a tendency to overlook the fact that we have incredibly little information as to precisely how many hospital beds we require. The figure suggested in the early days of the National Health Service was around five hospital beds per 1000 population, and the hospital enthusiasts make much play with the fact that the present national average is only 3.1 per 1000 population. According to the Nuffield Provincial Hospitals Trust, however, even this latter figure is too high. In a report published in 1955, based upon a survey in Norwich and Northampton, the Trust suggested that a ratio of about two beds per 1000 population was adequate. That this figure was not very far off the mark is suggested by another report the Trust has just published, based upon a survey carried out in the ship-building town of Barrow. This new report indicates that for Barrow the appropriate ratio of beds is 2.5 per 1000 population. In these price-conscious days, when the mounting cost of the National Health Service is causing so much concern, the significance of these findings is admirably summed up by the authors of the Trust's report: "At present costs (at £5000 per bed in new hospital construction and £1500 for a new council house) even to provide one bed per 1000 population in England and Wales, a total of 45,000 beds, would have meant building 150,000 fewer houses. Again the cost of these beds would represent about one-third of the annual running costs of the National Health Service."

TEENAGER V.D.

A discussion on "venereal disease in the teenager" at the recent annual congress of the Royal Society of Health has focused public attention on a problem which has been worrying many doctors and social workers during the past few years. Dr. A. J. King reported that during the year ended June 30, 1959, 6255 new cases were seen at the Whitechapel Clinic, one of the largest venereal disease clinics in London. Two-thirds of these were infectious cases, and 490 of

these were in teenagers. The over-all picture showed that the proportion of women attending the clinic who were under the age of 21 has risen from 16% in 1936 to 21% in 1959. Comparable findings are included in an as yet unpublished study by the British Co-operative Clinic Group, based upon the figures from 147 venereal disease clinics in England and Wales. These show a serious and rising incidence of infection in 1958, compared with 1957, among young people in the 18-19 age-group, which was greater than that for any other group and well above the average increase for the country as a whole. Similarly, at Holloway Prison, teenagers are forming an increasing proportion of prostitutes who are admitted.

According to another speaker, the number of women attending one venereal disease clinic during last year was about double that attending 20 years ago. One in five of those attending was a girl with "a nice office job", compared with one in 25 before the war. It was this same speaker who reported that "most girls admitted to initial sexual acts between the ages of 13 and 16".

WILLIAM A. R. THOMSON

London, May 1960.

OBITUARIES

DR. PIERRE BEGIN, aged 59, died April 18 in Hull, Quebec. Born at St-Louis-de-Pintendre, Lévis, he was educated at Ste-Anne-de-Beaupré and obtained his medical degree from Laval University in 1927. Dr. Bégin practised in Rimouski and Hull.

Surviving are his widow, two sons and three daughters.

DR. JOHN STANHOPE GLADWIN, aged 85, died March 20 in Vancouver. Born in Nova Scotia, he graduated from the University of Pennsylvania. He practised in the coal mining towns of Crowsnest and Fernie, B.C., served in the Boer War and First World War, and practised in Vancouver until his retirement in 1944.

Dr. Gladwin is survived by his widow.

DR. LAURENT GODIN died April 16 in Montreal. Born in 1887 in Côte St-Paul, he received his medical degree from the University of Montreal in 1911. He practised general medicine in Montreal for over 40 years.

Surviving are his widow and one son.

DR. CECIL ULYSSES HOLMES, 85, died April 18. Born in Selkirk, Ont., he graduated from the University of Toronto in 1898. He practised in Hagersville, was medical superintendent of Six Nations Indian Reserve and established a practice in Edmonton, Alta., in 1911. He served as a medical officer in the Canadian Expeditionary Force, returned to private practice in 1918, and was a lecturer in obstetrics at the University of Alberta Medical School. He retired from practice in 1937 and became district administrator of the Department of Veterans Affairs.

Dr. Holmes is survived by one son.

PROVINCIAL NEWS

BRITISH COLUMBIA

In April an experimental drive was made by Medical Services Incorporated (M.S.I.), whereby everybody, even persons over 65, was offered the privilege of obtaining individual coverage against illness. This is an entirely new departure for M.S.I., which so far has insured only groups of from three to nine persons under the age of 65. The drive has met with marked success, and some 2800 applications have been received in two weeks. This group will be watched carefully for a year, to see how the experience operates. Coverage may apply to single persons, couples, and families of three or more, with varying charges.

The campaign of the B.C. Division of the Canadian Cancer Society, aimed at education of the public in cancer prevention, is attracting wide interest everywhere in the province. An instance is the meeting of the Burnaby Unit, early in April, when Dr. David A. Boyes, assistant director of the cytology department of the B.C. Cancer Foundation, addressed a packed audience on "Time and two women." Many were turned away for lack of space. This campaign is directed particularly to women.

Grants amounting to \$146,000 have been made by the National Cancer Institute of Canada to 16 doctors in B.C., for cancer research. All but one of the projects contemplated will be carried out at the University of British Columbia. Dr. W. B. Chung of Victoria will carry on his share of the research at the Vancouver General Hospital.

One major project is that being carried on in the laboratories of the B.C. Cancer Institute, under Dr. Marvin Darrach, head of U.B.C.'s biochemistry department, Dr. D. Boyes and Dr. D. K. Ford. A new \$225,000 laboratory is now in use. The project has chiefly to do with cancer of the cervix in women; an active campaign of education is being conducted by the B.C. Cancer Institute to enlist the cooperation of doctors, and of the women of B.C., in annual check-ups.

A prominent worker in this laboratory is Dr. Nelly Auersperg, a native of Vienna and a graduate of the University of Washington, who is one of those obtaining grants. Her work will be chiefly concerned with cytopathology, and screen tests for cervical cancer.

Dr. J. F. C. Anderson (Jack Anderson) of Saskatchewan appeared before the Vancouver Medical Association on April 5, at the invitation of the Executive, to report on the present status of events in Saskatchewan, where the CCF Government is endeavouring to introduce a health insurance plan. He gave a full account of the reactions of the medical profession in that province, and of the steps it is taking to safeguard the practice of medicine.

Workmen's Compensation Commissions across Canada are working towards the establishment of a central agency where the name of any person exposed to a heavy dose of radiation will be recorded.

As regards British Columbia, the Workmen's Compensation Commission will seek to have more

stringent and up-to-date regulations embodied in the Provincial Workmen's Compensation Act, regarding the handling of radioactive materials.

A federal grant of \$39,400 has been given to the department of psychiatry of the University of British Columbia, to assist in the development of extensive postgraduate study at the university, which will help to train psychiatrists for provincial mental hospitals and community clinics.

The Annual Clinical Meeting of the B.C. General Practitioners' Section of the C.M.A., B.C. Division, was held at Harrison Hot Springs from March 29 to April 2. The attendance was good, and the clinical program excellent. Dr. Gordon Wilson of Kelowna, the President of the Section, was in charge.

Dr. Bob Stanley is President for the coming year—and the 1961 meeting will be held in Vancouver.

J. H. MACDERMOT

MANITOBA

Dr. Arthur Sutherland, head of the department of obstetrics and gynaecology, Southwestern District Hospitals, Glasgow, visited Winnipeg on his return from a trip to medical centres on this continent. He spoke to third-year students at the University of Manitoba on April 19 on "Genital tuberculosis in the female" and in the evening to the Section of Obstetrics and Gynaecology of the Winnipeg Medical Society on "Placentography". Using a special technique worked out by the radiologist of his hospital, he found it possible to achieve 98% success in locating the placenta with a single lateral plate.

Dr. Moran Campbell of Middlesex Hospital, London, spoke in the Medical College on April 26 on "Proprioceptive aspects of breathing and the stabilization of tidal volume".

At the recent annual meeting of the American College of Physicians, held in San Francisco, Dr. Victor J. H. Sharpe of Brandon, son of Dr. H. S. Sharpe, F.A.C.S., received the qualification of Fellow of the American College of Physicians.

ROSS MITCHELL

QUEBEC

The Montreal Medico-Chirurgical Society concluded this year's program with an annual clinical evening held at the Royal Victoria Hospital on Monday, April 25. The evening began with an excellent buffet supper at 6.30 p.m., with an estimated attendance of about 300 including many out-of-town visitors. In addition to the members of the Society, invitations had been extended to La Société Médicale de Montréal, the medical students of McGill University and the University of Montreal, and residents and interns of all Montreal hospitals.

The theme of the meeting was postgraduate education, and the 64 scientific exhibits gave an opportunity to review recent advances. Most, if not all, of the exhibits presented this knowledge in such a way that it could be utilized for the actual treatment of patients. The postgraduate board of the Royal Victoria Hospital, the organizers of this outstandingly successful meeting, are to be congratulated on a job well done.

The same evening, Monday, April 25, the Montreal Physiological Society also held its annual meeting at the Ayerst Research Laboratories in Ville St-Laurent. The new research laboratory buildings were open from 7 to 8.15 p.m. for inspection. Among other items, a new slate of officers for the coming year was elected, including Dr. Eleanor Harpur, president; Dr. E. Page, vice-president; and Dr. J. Parker, secretary. The main part of the program was an address by the retiring president, Dr. A. D'Iorio, whose subject was "Catabolic pathways of catecholamines". He first spoke on the nature of the granules within the cells of the adrenal medulla which contain the adrenaline. There is evidence to indicate that these granules are true sacs with a membrane and that the adrenaline within the granules is in combination with ATP and an alpha globulin. Dr. D'Iorio and his associates have conducted extensive studies on the nature of these granules, their functions and how they participate in the adrenaline-release mechanism. In the second part of his address, Dr. D'Iorio spoke on the metabolism of adrenaline and the fate of adrenaline in the body. Their results are still somewhat incomplete to explain the mechanism or to present a reasonable scheme of this catabolic pathway.

The Quebec Camp for Diabetic Children Inc. will open its third season on August 15, and will run for a two-week period. It has been possible for the directors to secure the facilities and staff of Camp Wilvaken for this period. The camp is situated on Lake Lovering, six miles from Magog, Que. It is hoped that both English-speaking and French-speaking diabetic children will avail themselves of the opportunity to attend camp. Physicians interested in sending their patients are requested to apply to Dr. Mimi M. Belmonte, The Montreal Children's Hospital, 2300 Tupper Street, Room 478.

The annual meetings of two of Montreal's English-speaking hospitals were held in the last two weeks of April. Both emphasized extensive building and renovation programs now in progress and partly completed. The Verdun Protestant Hospital cared for more patients in 1959 than in any previous year in its history. Construction on the \$4,000,000 building and renovation program has begun, which will include a 150-bed medical-surgical unit and 100-bed continuous-care building. The cost will be covered through federal-provincial grants and about \$750,000 raised by the recent building fund campaign. The annual report presented by Dr. Charles Roberts, medical superintendent, was very optimistic throughout, including the section dealing with problems of the older patients. Any feeling of a tendency towards hopelessness is offset by the fact that last year one-fifth of patients over 65 admitted were discharged during the same year.

The annual report of the Queen Elizabeth Hospital, presented by its medical director, Dr. Harold R. Griffiths, showed partial completion of their building and alterations program but also reported a slight increase in the annual deficit, from \$59,065 for 1958 to \$75,925 in 1959. Beginning about May 1, the hospital expected to move patients into the new wing. On that day the interns and the outpatient department moved into new quarters provided in the old residence for nurses. The new nurses' residence

is completed and plans are under way to establish in 1961 a school for nursing assistants which will be run in conjunction with, but quite separate from, the existing school of nursing.

Dr. Donald Ross, associate professor of psychiatry and associate professor of industrial medicine at the University of Cincinnati, delivered the fifth annual Françoise Boulanger Memorial Lecture at the Montreal Children's Hospital on March 26. He spoke on "Psycho-analytic observations on the emotional situation of the group psychotherapist".

Dr. Rolland Simard has been appointed chief of the department of gynaecology at Notre-Dame Hospital in Montreal. He assumes the post held for so many years by our illustrious friend, the late Dr. Léon Gérin-Lajoie.
A. H. NEUFELD

NOVA SCOTIA

Dalhousie medical graduates, their wives and guests from Eastern Canada and the United States attending the C.M.A. meeting in Banff, in June, will have an opportunity to meet with Dalhousie graduates from Western Canada and the United States who will be attending the convention. A reunion, in the form of a reception and buffet, has been arranged to take place at the Banff School of Fine Arts at 5.30 p.m. on the evening of June 16. This informal gathering will be under the chairmanship of Dean Walter MacKenzie of the University of Alberta, with Dr. Donald Ramsay of Calgary acting as chairman. To Dalhousians, this should prove an added attraction in the extensive social program at the meeting. If you are planning to be there, drop a card to that effect to Dr. Ramsay, 214 6th Avenue West, Calgary.

PUBLIC HEALTH

SURVEILLANCE REPORTS OF
EPIDEMIC OR UNUSUAL
COMMUNICABLE DISEASES

PARALYTIC POLIOMYELITIS

For the period January 1 to April 9, 1960, 76 cases of paralytic poliomyelitis have been reported in Canada. British Columbia accounts for 34 cases; Alberta 13; Quebec 16, Newfoundland 6 and New Brunswick 4. Nova Scotia, Ontario and Manitoba have reported one case each.

The cumulative total to this date for the years 1949 to 1960 is presented below:

Years	Cumulative total to April 9
1949.....	9
1950.....	39
1951.....	11
1952.....	19
1953.....	39
1954.....	64
1955.....	39
1956.....	30
1957.....	16
1958.....	13
1959.....	20
1960.....	76

SUMMARY OF REPORTED CASES OF NOTIFIABLE DISEASES IN CANADA*
ISSUED BY THE PUBLIC HEALTH SECTION, DOMINION BUREAU OF STATISTICS

Disease	Week ended (1960):				Cumulative total since beginning of year	
	April 2	April 9	April 16	April 23	1960	1959
Brucellosis (Undulant fever).....(044)	2	2	1	1	18	24
Diarrhoea of the newborn, epidemic.....(764)	2	—	—	—	15	26
Diphtheria.....(055)	—	—	1	—	11	13
Dysentery:						
(a) Amœbic.....(046)	—	—	—	—	1	2
(b) Bacillary.....(045)	63	59	31	34	944	283
(c) Other and unspecified.....(047, 048)	6	4	3	—	113	11
Encephalitis, infectious.....(082.0)	—	—	—	1	7	2
Food poisoning:						
(a) Staphylococcus intoxication.....(049.0)	—	—	—	—	236	5
(b) Salmonella with food as vehicle of infection.....(042.1)	12	6	9	6	160	102
(c) Unspecified.....(049.2)	3	—	—	—	11	39
Hepatitis, infectious (including serum hepatitis).....(092, N998.5)	83	71	121	79	2,140	2,189
Meningitis, viral or aseptic.....(080.2, 082.1)	5	1	1	1	67	21
Meningococcal infections.....(057)	—	1	5	2	58	73
Pemphigus neonatorum (Impetigo of the newborn).....(766)	—	—	—	—	4	1
Pertussis (Whooping cough).....(056)	134	147	103	81	1,970	1,946
Poliomyelitis, paralytic.....(080.0, 080.1)	7	8	1	—	77	19
Scarlet fever and Streptococcal sore throat.....(050, 051)	766	577	471	307	11,925	9,804
Tuberculosis:						
(a) Pulmonary.....(001, 002)	47	80	98	63	1,444	1,933
(b) Other and unspecified.....(003-019)	25	27	21	32	414	593
Typhoid and Paratyphoid fever.....(040, 041)	3	8	8	12	122	261
Venereal diseases:						
(a) Gonorrhœa.....(030-035)	296	222	276	248	4,455	4,305
(b) Syphilis.....(020-029)	34	40	38	21	595	620
(c) Other†.....(036-039)	—	—	—	—	3	2

*Figures for the Yukon are received four-weekly and are, therefore, shown in the cumulative totals only.

†Including chancroid, granuloma inguinale and lymphogranuloma venereum.

INFLUENZA

A severe outbreak of influenza has been reported in an old people's home in Edmonton, Alberta involving some 30 persons. The matron and a 74-year-old female inmate were seriously ill and had to be sent to hospital. Two men died. A hæmagglutinating virus has been isolated from the throats of five patients, including the two who died. The serological titre of a hospitalized patient showed a rise against influenza virus type A from 1:16 to 1:25.

In five more army personnel at Curry Barracks in Calgary and in one case previously reported from Jasper, a significant rise in titre against influenza virus type A has been demonstrated.

CRYPTOCOCCOSIS

A case of meningitis due to *Cryptococcus neoformans* (*Torula histolytica*) affecting a 24-year-old R.C.M.P. officer has been reported from New Westminster, B.C. The patient is seriously ill and is at present in the Royal Columbian Hospital. The onset occurred on April 7 and the disease was diagnosed on April 12 by isolation of the organism.

MALARIA

One case of malaria in an adult female has been reported from the North Fraser Health Unit, British Columbia.

TRICHINOSIS

Quebec.—Five cases of trichinosis have been reported from the province of Quebec for the week ending April 16, and five cases for the week ending April 23, 1960, bringing the total to date to 27 cases.

INDIAN AND NORTHERN HEALTH SERVICES

The outbreak of influenza-like disease reported previously at Coppermine, N.W.T., has now involved about 250 persons, Eskimos and whites. About 30 patients have been

admitted to hospital locally. No deaths have been reported and the majority of those affected are recovering well.

Outbreaks of influenza-like illness have also been reported from:

Bathurst Inlet, N.W.T.—About 60 Eskimo cases, involving the whole population. Six patients were evacuated to Cambridge Bay with pneumonia.

Cambridge Bay, N.W.T.—About 60 Eskimos. Seventeen patients had pneumonia and were admitted to hospital at the nursing station.

Spence Bay, N.W.T.—About 60 Eskimo cases and one death.

Gjoa Haven, King William Island, N.W.T.—Fifteen cases have occurred, including two in Roman Catholic priests.

Trout Rock, Yellowknife, N.W.T.—About 56 people have been affected, all Indians.

Old Crow, Yukon Territory.—The whole village population has been affected. Old people were more seriously ill and eight cases of pneumonia occurred. There were no deaths.

INFLUENZA:

International Reports

United States.—No further reports of epidemic influenza have come to the attention of the Surveillance Section, Communicable Disease Center, since approximately mid-March. It is likely that the peak of national morbidity due to the disease was reached in late January or early February, with a gradual decline since that time.

From the 45 States in which clinical influenza or isolation of influenza virus has been reported this season, influenza virus A2 was identified in 37 States, virus A in 6 States, and virus A1 in 3 States, and virus B was isolated in 2 States. It is apparent that type A2 influenza virus was the etiological agent in the vast majority in the epidemic that occurred in the United States during the winter months of 1960.

Epidemiology Division,
Department of National Health
and Welfare, Ottawa.

April 23, 1960.

ABSTRACTS from current literature

MEDICINE

Gastric Acid Secretion in Diabetes Mellitus.

I. N. MARKS, C. R. SHUMAN AND H. SHAY: *Ann. Int. Med.*, 51: 227, 1959.

The status of gastric acid secretion in 41 patients with diabetes mellitus was investigated by means of the augmented histamine test. The mean secretory responses in both the male and the female groups of patients with diabetes were found to be comparable to the mean values reported in respective groups of normal subjects. Acid secretion did not appear to be influenced by the severity or duration of the disease. Achlorhydria was found in two patients, and a further two had evidence of duodenal ulceration. Diabetic diarrhoea was usually, but not invariably, associated with low levels of acid secretion.

The results of this study of gastric secretion did not provide any evidence for the view that acid secretion tends to be low in diabetics, or for the belief that diabetes mellitus is, *per se*, a cause of progressive diminution of acid secretion.

S. J. SHANE

Effect of Acetylcholine on Pulmonary Vascular Resistance in a Patient with Idiopathic Pulmonary Hypertension.

R. J. MARSHALL, H. F. HELMHOLZ, JR. AND J. T. SHEPHERD: *Circulation*, 20: 391, 1959.

Acetylcholine chloride was infused at a rate of 2 mg. per minute into the outflow tract of the right ventricle of a 48-year-old woman who had idiopathic pulmonary hypertension. A steady cardio-respiratory state was achieved by this continuous infusion. The mean pulmonary artery pressure decreased from 56 to 25 mm. Hg, and the pulmonary blood flow increased slightly. The pulmonary vascular resistance was correspondingly reduced. The degree of oxygen saturation of systemic arterial blood, the systemic arterial pressure and the heart rate were unchanged. These results demonstrate that "constriction of pulmonary vessels played an important role in maintaining the pulmonary hypertension in this patient. The mechanism by which the constriction originates and is maintained is unknown.

S. J. SHANE

Treatment of Pulmonary Tuberculosis with Isoniazid and Pyrazinamide: Experience in 114 Cases.

M. J. SMALL: *Dis. Chest*, 36: 265, 1959.

One hundred and fourteen patients were treated with the combination isoniazid-pyrazinamide for periods of one to 25 months. Of eight showing no change on roentgen evaluation at the fourth month of treatment, it is considered significant that all had achieved bacteriological "conversion", and that five had persistent open cavity with negative sputum. Of 58 moderately and far-advanced cases, 22 became markedly improved, 17 moderately improved, 10 slightly improved, and only one worsened. Of 55 with moderate and far-advanced disease treated for at least four months, 80% achieved bacteriological negativity during the first two months, the vast majority doing so during the first month of treatment. An additional 13 "converted" during the third and fourth months. Four patients (7%) remained positive, and they all became resistant to isoniazid within two months. Of 19 cases with a cavitary component of 4

cm. or more, 11 became "open negative," four became "closed negative," and four remained "open, positive, resistant".

Evidence of hepatic toxicity was obtained in 15% of 114 cases from an abnormal liver function test. Clinical hepatic involvement as well occurred in an additional 4%. There was one death in association with jaundice; its relationship to pyrazinamide seems doubtful. All evidence of hepatic toxicity, clinical or laboratory, appeared in a scattered fashion during the first 10 months of treatment; no toxicity was detected in 12 cases which received pyrazinamide for 10-25 months.

The achievement of bacteriological negativity with persistence of open large cavity appears to happen much more often with isoniazid-pyrazinamide than with various combinations of streptomycin, isoniazid and para-aminosalicylic. The major disadvantage of isoniazid-pyrazinamide therapy is the hepatotoxicity of pyrazinamide, which manifests itself in most of the cases only by abnormal laboratory tests. Because of this it is felt that isoniazid-pyrazinamide should be used only in those patients in whom frequent liver function studies can be carried out. Further effort should be directed towards finding more sensitive laboratory indices of early pyrazinamide toxicity.

S. J. SHANE

Pericardiectomy for Massive Recurrent Pericardial Effusion.

R. J. JAFFE AND H. KALLMAN: *Ann. Int. Med.*, 51: 363, 1959.

The clinical syndromes produced by chronic constrictive pericarditis and pericarditis with massive effusion may be identical. Removal of large amounts of fluid from the pericardial cavity is stated to be a safe procedure. In the case of chronic idiopathic pericarditis with massive effusion presented, 2150 c.c. of fluid was removed at one time, and a total of 3880 c.c. in less than 48 hours. As a diagnostic aid, induced pneumopericardium is of value in searching for neoplastic lesions of the pericardium or the epicardial surface of the heart. Should medical work-up prove negative, thoracotomy seems justified. Early surgical intervention is urged. However, the good result obtained in this patient suggests that surgery is warranted even after prolonged tamponade and despite cytological evidence suggestive of malignancy.

S. J. SHANE

Rauwolfia Alkaloids in Diabetic Hypertensive Patients.

A. S. COHEN *et al.*: *Ann. Int. Med.*, 51: 238, 1959.

Reserpine was administered orally to 28 patients with diabetes mellitus and relatively fixed hypertension of greater than five years' duration, and a cruder rauwolfia preparation to a group of 10 patients. The latter group was studied by the double-blind control technique.

In the first study, diabetic status was not significantly altered in any of 10 patients maintained on diet alone. Of 18 on insulin therapy, insulin dosage was decreased slightly (10 units) in three patients and moderately (20 units) in one. It was increased (30 units) in one patient. No significant weight changes accompanied these alterations. The double-blind study showed no effect on the status of the diabetes. Hypotensive effects were seen in both series of patients, even in the presence of "fixed" hypertension of long duration.

No changes in body weight could be attributed to either reserpine or rauwolfia.

S. J. SHANE

Effects of Infusion of Acetylcholine on Pulmonary Vascular Resistance in Patients with Pulmonary Hypertension and Congenital Heart Disease.

J. T. SHEPHERD *et al.*: *Circulation*, 20: 381, 1959.

In this study acetylcholine was administered by constant-rate infusion into the pulmonary arteries of 11 patients with pulmonary hypertension associated with atrial or ventricular septal defect. The oxygen consumption, oxygen saturation in the pulmonary artery and systemic arterial blood, and the pulmonary artery pressure were recorded continuously before, during and after the infusion. These data were used to determine changes in total pulmonary resistance during infusion of acetylcholine.

All six of the patients with atrial septal defects showed some decrease in resistance during acetylcholine infusion. If the pulmonary resistance when the patient was breathing air is taken as 100%, the decrease was 23% (range 15 to 51) with infusion of acetylcholine alone, 29% (range 9 to 33) on breathing oxygen and 43% (range 27 to 60) on breathing oxygen and receiving acetylcholine.

Of the four patients with only ventricular septal defect, only one did not respond to either oxygen or acetylcholine. For the remainder the average percentage decrease in resistance with acetylcholine while breathing air was 31% (range 10 to 69), while breathing oxygen 33% (range 25 to 66), and while breathing oxygen and receiving acetylcholine 57% (range 35 to 74). One patient with both an atrial and a ventricular septal defect showed no response. As there was no evidence of a decrease in left atrial pressure with acetylcholine, these changes in total pulmonary resistance presumably represent an actual reduction in pulmonary vascular resistance.

It is concluded that active constriction of pulmonary vessels is an important factor in maintaining the high resistance to pulmonary blood flow found in some patients with congenital heart disease. S. J. SHANE

Effect of Mitral Valvulotomy on Tricuspid Insufficiency Associated with Mitral Stenosis.

P. F. ANGELINO, B. LO BUE AND V. LEVI: *Circulation*, 20: 360, 1959.

Twenty patients who had mitral valve disease with tricuspid insufficiency and who were selected for mitral commissurotomy on the basis of clinical evidence of advanced heart disease were studied before and after surgery, in order to evaluate further modifications in cardiocirculatory function. According to the type of mitral disease, two groups of patients were distinguished: in 13, pure mitral stenosis was demonstrated, while in seven mitral stenosis was associated with mitral insufficiency. An additional subdivision was made between subjects with moderate pulmonary hypertension and those with pulmonary arteriopathy among patients with pure mitral stenosis.

Good results from operation were obtained in a few patients with severe pure mitral stenosis, moderate pulmonary hypertension, and functional tricuspid insufficiency. Very little improvement was observed in patients with mitral regurgitation, pulmonary arteriopathy, or organic tricuspid insufficiency. Two patients in this group died.

The myocardial response to the mechanical improvement brought about by mitral commissurotomy seems to be an important factor in the subsequent course of the disease. S. J. SHANE

SURGERY

The Solitary Circumscribed Pulmonary Lesion due to Bronchogenic Carcinoma: Three-year Follow-up Study of 94 Surgically Treated Patients.

J. W. VANCE *et al.*: *Dis. Chest*, 36: 231, 1959.

In 94 surgically treated patients who had bronchogenic carcinoma seen on thoracic roentgenography as a solitary circumscribed pulmonary lesion, the resectability rate was 90% and the hospital mortality rate was 5.3%. Cytological examination of the sputum was of definite value in the preoperative diagnosis of the uncalcified solitary pulmonary lesion. The presence or absence of thoracic symptoms seemed to be the most significant prognostic variable studied. The overall three-year survival rate was 36.6%. There seems to be no essential difference in the three-year survival rates for resectable bronchogenic carcinoma whether it presents on the thoracic roentgenogram as a solitary circumscribed pulmonary lesion or not.

The writers emphasize that present surgical treatment of bronchogenic carcinoma must be vigorously pursued, a maximal effort being directed at early diagnosis and early surgical resection. S. J. SHANE

Coarctation of Aorta with Proximal Aortic Dilatation and Calcific Atheromatous Degeneration Corrected by Endarterectomy.

P. J. FLYNN AND A. A. KATTUS: *J. Thorac. & Cardiovasc. Surg.*, 38: 369, 1959.

Dilatation and degenerative changes of the aorta proximal to a coarctation are frequent findings in the surgical repair of this congenital anomaly. When these changes in the aortic wall are pronounced, the difficulties of operative correction and the incidence of postoperative hæmorrhage are appreciably increased. The accepted procedure of resection and anastomosis in such cases presents a formidable surgical problem, generally accompanied by a high operative mortality.

In the case reported, the proximal aorta as well as the coarctation segment was involved with calcific atheromatous degeneration. The constricted segment was restored to an adequate lumen by a longitudinal aortotomy and endarterectomy. This operative approach, although not applicable in the majority of cases of coarctation, is recommended as an alternative procedure in selected patients. S. J. SHANE

Ischæmic Necrosis of the Proximal Gastric Remnant Following Subtotal Gastrectomy.

P. P. JACKSON: *Ann. Surg.*, 150: 1071, 1959.

The blood supply to the stomach via the four main arteries, the surrounding arterial net, and the presence of a rich intramural plexus with arteriovenous anastomoses make ischæmic necrosis very rare even after extensive resections and ligation of most of the blood supply. But gangrene of the gastric stump followed an 85% gastric resection for high gastric ulcer in Vancouver. At autopsy, there was atherosclerosis of the splenic artery and vasa brevia. Variations in the origin of the phrenic arteries from the left gastric may have been a factor.

It is recommended that when a high gastrectomy is performed, note should be made of the bleeding from the gastric stump and its colour. A drain might have made the diagnosis clear when the patient suddenly went into shock a day and a half after operation.

BURNS PLEWES

Traumatic Dislocation of the Hip in Children.K. S. MORTON: *Brit. J. Surg.*, 47: 233, 1959.

There are 129 cases of traumatic dislocation of the hip in children under 16 in the English medical literature and seven more are reported from the Vancouver General Hospital.

The most usual injury is a weight falling on the back while the child is squatting or on all fours. Most were posterior dislocations and all were reduced by manipulation. There were few complications and results were excellent, both with immediate weight-bearing and prolonged immobilization. Avascular necrosis occurs in 10%, though there was none in the Vancouver cases.

BURNS PLEWES

Surgical Treatment of Lesions Producing Arterial Insufficiency of the Internal Carotid, Common Carotid, Vertebral, Innominate and Subclavian Arteries.M. E. DeBAKEY, E. S. CRAWFORD AND W. S. FIELDS: *Ann. Int. Med.*, 51: 436, 1959.

Arteriography was performed in 305 patients with arterial insufficiency of the cerebrum and upper extremities. Extracranial arterial occlusion was demonstrated in 122 patients (40%), 106 of whom were submitted to operation. Of the 174 lesions in the latter cases and located in the internal carotid, vertebral, innominate, common carotid and subclavian arteries, 149 lesions were explored surgically, and 136 obstructive lesions in 93 patients were found to be segmental in nature and amenable to restorative operation. The remaining patients had extensive complete occlusion of the internal carotid or vertebral arteries, and, in view of the duration of occlusion, were not considered to be operable.

The proximal forms of the disease were evident clinically by the manifestations of arterial insufficiency of the cerebrum and upper extremities. The distal occlusions were manifested by cerebral arterial insufficiency. Owing to the limitations of accurate localization of the lesion on clinical grounds, all patients were studied by means of arteriography. Lesions occurring in the great vessels arising from the aortic arch were operable, regardless of the location and extent of occlusion. Incomplete occlusions of the internal carotid and vertebral arteries were similarly amenable to operation. Complete occlusions of the latter vessels were rarely operable unless explored soon after onset of symptoms.

Treatment of these cases was directed toward restoration of normal circulation, and, to achieve this objective, two types of procedure were employed, endarterectomy and end-to-side by-pass graft. Endarterectomy was employed in the treatment of well-localized lesions, and the more extensive occlusions were by-passed by using a suitable arterial substitute. Endarterectomy was performed in 85 lesions, and graft by-pass was employed in the treatment of 51 lesions. A pulsatile circulation was restored in the treatment of 133 lesions. Circulation was restored in all cases of lesions involving the great vessels arising from the aortic arch, in 97% of those with operable lesions of the internal carotid artery, and in 66% of those with occlusions of the vertebral artery.

All patients with lesions of the great vessels were completely relieved, and the majority of patients with lesions of the internal carotid and vertebral arteries were either relieved or improved. These patients have

been followed up for periods of over five years, and the success achieved by operation has been well maintained.

S. J. SHANE

THERAPEUTICS**Some Observations on a Sedative and a Tranquillizing Agent.**C. H. SCHEIFLEY: *Proc. Staff Meet. Mayo Clin.*, 34: 408, 1959.

Some 400 hospitalized cardiac patients exhibiting varying degrees of anxiety and tension were treated with a newly developed "relaxing agent", plexonal. Plexonal was greatly superior to any previous sedative-type medication used. It brought about an almost dramatically increased ease in the handling of the anxious and disturbed cardiac patient, and it greatly reduced the number of problems arising from enforced reduction of activity and rest in bed. It had the added effect of combating depression. It reduced or eliminated insomnia in virtually all the patients when an adequate daily dose was used.

In an effort to find a medication the therapeutic effect, as well as the incidence and severity of side effects, of which could be predicted, two preparations, meprobamate and plexonal, were administered to 72 patients. Plexonal was preferred (superior therapeutic effect) by 73.7% of the patients, whereas 11.1% preferred meprobamate, a ratio of 6.6 to 1. Plexonal produced side effects, consisting of drowsiness or mild headache, in 5.6%. Meprobamate produced adverse side effects in 30.5%. In 26.4% these reactions were severe, incapacitating or even dangerous. The use of plexonal had to be stopped in two instances because of development of a skin rash. Two patients experienced severe anaphylactic-shock type of reaction after the first dose of meprobamate.

It can be concluded that, if the patient is instructed carefully in adjustment of the dose of plexonal, he can be sent home with a prescription for this agent with confidence that in the great majority of cases good results will be obtained. At the same time there will be no risk of serious side effects, and the incidence of mild side effects will be low.

S. J. SHANE

INDUSTRIAL MEDICINE**Fatal Nephropathy during Edathamil Therapy in Lead Poisoning.**H. G. BRUGSCH: *A.M.A. Arch. Indust. Health*, 20: 285, 1959.

This review analyzes available reports in regard to possible toxic effects of edathamil, indicates methods of study which may help to clarify its renal action, and suggests precautions for its use. Although concerned essentially with edathamil, it includes reference to toxicity observed in the use of Sodium Versenate and of Versenol.

Since 1956, significant evidence of renal damage in both animals and humans treated with edathamil has been shown. It has long been recognized that lead intoxication causes or contributes to renal disease. Analysis of data now available indicates that the high load of lead excreted predominantly through the kidneys after intravenous CaNa_2 edathamil in lead poisoning adds another burden to the renal tubular system. It suggests further that both lead and calcium could act as a tubular-damaging substance. It can

therefore be assumed that the kidney if diseased in patients with lead poisoning will show a particular susceptibility to edathamil.

Further studies on patients with lead poisoning, particularly those under treatment with chelating agents, are needed to establish the relation of "free" lead to lead Versenate in the body tissues, especially blood, and to clarify the renal clearance of lead Versenate.

In the author's opinion edathamil is still a good drug to be used when needed, but it may soon be replaced by a safer chelating agent. Edathamil should be given only in conjunction with proper evaluation of the patient's renal status before, during, and after therapy. This should include a renal function test (phenolsulfonphthalein (PSP) and concentration-dilution), non-protein nitrogen or blood urea nitrogen determination, and examination of at least two urinary sediments at the beginning of therapy and repeated whenever necessary. Courses of therapy by slow intravenous infusion should be short (probably not more than three days) and widely spaced (more than two weeks apart), and the daily total dose should not exceed 2 g. in adults.

MARGARET H. WILTON

Return to Work after Surgery—an Industrial Study.

A. J. FLEMING: *J. Occup. Med.*, 1: 531, 1959.

Despite the complexity of today's surgical procedures, recent medical practice has led to shortened hospital stay. Industry is concerned with the total period of an employee's absence from work, on account of employee benefit plans. It is important that the period of disability in each case be kept to the lowest possible

level consistent with good surgical care and employee welfare.

The purpose of the study reported was to determine whether early ambulation, shortened hospital stay, and shortened convalescence after the more common surgical procedures have reduced the period of disability. Information was obtained from the accident and health insurance claims for non-occupational illness during 1956, of some 90,000 employees in a large American company. The data were processed by the Biostatistics Section of the Company Medical Division.

Disability data from appendectomy and hernioplasty are compared with similar data which had been recorded by other investigators over a period of about 40 years. From this comparison it would appear that improved surgical technique, early mobilization, and in-plant medical supervision have resulted in earlier return to work, despite the fact that loss of income is no longer an important incentive to return early. Further data present information about disability in 1956, following surgery for six common conditions. They indicate that the period of convalescence after surgery is influenced by sex and payroll classification, but it is not influenced by the geographical distribution of employees or by the length of hospital stay after surgery.

Attention is drawn to the role of the well-trained and experienced industrial physician, who is in an excellent position to know the requirements of each job and to advise on fitness for work. It is suggested that this decision be left to him once the surgeon is satisfied about the surgical recovery.

MARGARET H. WILTON



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BOOK REVIEWS

LECTURES ON THE INTERPRETATION OF PAIN IN ORTHOPEDIC PRACTICE. A. Steindler. 733 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1959. \$20.25.

This is the last book of the renowned orthopaedist, Arthur Steindler. True to form, he corrected the last page proof on his death-bed, while suffering great pain himself from carcinoma.

Those familiar with Steindler's previous books will recall the heavy literary style, full of German grammatical forms, which makes them difficult to read. The present volume is no exception. The first seven "lectures" are devoted to generalized types of pain—e.g. joint pain, pain in muscles, tendons and fascial, bone pain etc. The remaining lectures describe the pain in every region of the skeleton, beginning with the spine and concluding with the foot, ankle and leg. The pattern in each chapter is essentially the same: introduction, anatomical review, and a detailed description of all the conditions which can cause pain in the area concerned.

Every page of this book contains some thought-provoking idea of interest to both the junior and advanced orthopaedist. It is a fitting memento of its distinguished author.

THE ESSENTIALS OF ROENTGEN INTERPRETATION. Lester W. Paul and John H. Juhl. 839 pp. Illust. Paul B. Hoeber Inc., Medical Book Department of Harper & Brothers, New York, 1959. \$25.00.

The authors claim to have produced a work whose detail lies between that of the elementary text and the massive reference set. To accomplish this—and they have done so with remarkable success—the writers have provided sufficiently concise and clear-cut descriptions of radiological appearances that they have been able to include discussion of an extremely wide variety of conditions. In many diseases the accuracy of diagnosis depends to a great extent on how the examination is carried out. While the minor refinements of roentgen technique are omitted from the text, general comments and guidance are given, particularly on patient preparation and general methods of carrying out examinations.

Facts concerning pertinent anatomy and pathology are briefly presented, but include the features important to most readers. Illustrations average over one per page and are of excellent quality. Bibliography is selective rather than massive.

This is one of the better new textbooks of general radiology and contains much of value to the student and the clinician as well as the specialist.

DAS ROENTGENSCHICHTBILD (The Tomographic Picture). A. Gebauer and others. 454 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1959. \$35.25.

In their monograph the authors attempt to cover the application of tomography in all medical specialties. Not since the publication of Greineder's "Tomography of the Lungs, Tracheo-bronchial Tree and Larynx" in 1941, has as comprehensive a text on this subject been published in the German literature. But numerous articles on the application of tomography to the investigation of different parts of the body have appeared in the world literature, as evidenced by the large bibliography attached to the text under review. More than half the text (250 out of 430 pages) is

devoted to the tomography of the chest. A detailed survey is made of the various pathological conditions as evidenced in tomographic studies. This includes the manifestations of disease in the trachea and the bronchial tree, tumours of the mediastinum, Boeck's sarcoid, pneumoconioses, and the investigation of the chest following pneumothorax, pneumolysis, thoracoplasty and plombage. A separate chapter deals with the application of tomography to the investigation of congenital and acquired diseases of the heart. Tomography of the abdominal viscera with and without the use of pneumoretroperitoneum is described in another chapter and so is the problem of tomographic localization of foreign bodies.

The use of tomography in the investigation of the skeletal system makes very interesting reading. Its value in the assessment of lesions of the petrous bone and mastoid is vividly illustrated, and so is its application to the lesions of vertebræ, hip joints and pelvic bones. The pneumoarthrograms of the knee joint are beautiful. The reproductions of the tomograms of the larynx and the accompanying explanatory drawings are among the best this reviewer has seen.

The chapter on theory and technique of tomography is very well written and includes also a description of special methods including straticopy (fluoroscopy of a section in motion), the latter without satisfactory results up to the present time. The book is abundantly illustrated. The prints are large and well explained through accompanying graphs and text. The graphic qualities of this book follow the tradition so well established by the house of Georg Thieme.

This text is highly recommended to the radiologist and to his colleagues in the other specialties of medicine and surgery who are interested in acquiring knowledge of an additional and very useful roentgen diagnostic procedure.

RECREATION IN TOTAL REHABILITATION. J. L. Rathbone and C. Lucas. 398 pp. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1959. \$10.50.

This book should prove challenging to those in the recreational field. It indicates ways in which recreation can be used best in the rehabilitation of patients with organic, motor, sensory, emotional, intellectual and mental illness or handicap. The book is also useful in that it indicates the important role of recreation to others in the rehabilitation program—doctors, nurses, and physical and occupational therapists.

The philosophy of recreation in rehabilitation is presented. The authors emphasize that recreational personnel who work with the ill and handicapped must do so only under specific instruction from the patient's physician and that each patient must have his individual prescription for recreation.

Various illnesses and handicaps are described in terms suitable for non-medical persons. Types of recreation are discussed in relation to each other, and many suggested programs are outlined.

The arrangement of the material is such that it makes for easy reading. Each chapter is divided into sections with headings, and the list of contents and the index are full and detailed.

This book could well be used as a textbook by the recreation worker and should also be in the library of every university which prepares those persons who may later be part of the rehabilitation team.

(Continued on page 1198)

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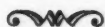
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(Continued from page 1196)

THE MICROCIRCULATION. Symposium on Factors Influencing Exchange of Substances Across Capillary Wall. Edited by S. R. M. Reynolds and Benjamin W. Zweifach. The University of Illinois Press, Urbana, Illinois, 1959. \$4.50.

This symposium presents three approaches to the problems of the morphology and function of capillaries. The first approach is based on the recent advances in the understanding of the capillary structure as elicited by the electron microscope. Emphasis is placed on the question of endothelial function in relation to transport of both fluids and particles across their cytoplasm. These considerations, although allowing for a clearer understanding of the structure of such vessels, fail to explain in dynamic terms the transport mechanisms involved. The second approach is that of the physiologist, using various models, i.e., semipermeable membranes, in the study of differential filtration processes. Little attempt, however, is made to correlate the conclusions arrived at by such methods with the morphological findings. The physiologists still envisage the existence of capillary "pores", an assumption not accepted by many electron microscopists. The third approach deals with the characteristics of the microcirculation and its physiological and pathological function in various locations, namely, retina, lung, skin and intestine.

The highly speculative approach to the problems at hand offers the research worker in the field of capillary permeability a means of formulating his own theories and explanations of the phenomena related to this object. This book is of only limited interest to the uninitiated.

DRINGLICHE CHIRURGIE BEIM SAEUGLING UND KIND (Urgent Surgery in Infants and Children). Dr. H. E. Grewe, Düsseldorf, Germany. 180 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1959. \$5.95.

This small but surprisingly complete volume reflects the experience of its author. No words are wasted on controversial theories or multiple procedures. This naturally makes the book somewhat dogmatic, but nevertheless authoritative.

The first part describes the treatment of acute diseases of the newborn; the second part deals with conditions requiring urgent surgery in infants and children. The text is arranged in topographical order, and at the end of the book the treatment of shock and collapse, replacement of electrolytes, feeding, and doses of antibiotics and other drugs are usefully discussed.

This is a very handy and clearly written book on the subject, with a sufficient number of informative illustrations.

THE CHILD IN HOSPITAL. A Study of His Emotional and Social Well-Being. Hedley G. Dimock. 236 pp. The Macmillan Company of Canada Limited, Toronto, 1959. \$3.75.

The author of this book introduces his topic with a brief review of the factors which affect the child as a person. Progressing to the emotional and social needs of the young patient in hospital and his reactions to his strange environment, Mr. Dimock reviews the effects of separation and the parents' role in the child's hospitalization. He emphasizes the parents' contribution in preparing the child for his admission to hospital,

and in giving the child emotional support during his stay in hospital by frequent, regular visiting, or "rooming-in" where it is feasible. There follows a discussion of desirable ways in which the various members of the hospital staff may meet their patient's needs and understand his reactions. Case histories provide a good basis for learning and discussion. The second half of the book is devoted to the child's social, educational and recreational needs.

Although somewhat unoriginal in its style, this book is easily read and understood. The early chapters would be of particular interest and value to student and graduate nurses. Used in conjunction with an in-service educational program, it could be helpful to the various members of the hospital team and provide a basis for staff discussion groups.

PEDIATRISCHER EKG-ATLAS (Paediatric Electrocardiographic Atlas). Wilhelm Heck and Joachim Stoermer, Göttingen, Germany. 230 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1959. \$18.55.

The principle of the museum collection as a means of teaching still remains necessary in the domain of electrocardiography. The theories which seek to account for the formation of the electrocardiographic patterns leave so much unexplained that clinico-pathological correlations remain essential to the interpretation of clinical electrocardiograms. Paediatric electrocardiography has lagged behind the adult type in accumulation and presentation of data. An atlas of this kind is therefore a welcome addition to modern medical literature. This reviewer wonders whether the authors would have been more consistent if they had omitted the section devoted to basic theory of electrocardiography. These 15 pages contain a compact treatment of the subject, too compact for the beginner and unnecessary for the initiated. The set of tables defining the measurements of the elements of the normal electrocardiogram in different age periods should prove very useful. If the authors had them available, it would have been appropriate to present measurements made in at least several single individuals from birth to puberty. Such observations must be rare, but are needed especially in normal subjects.

The main body of the book, from page 33 to page 221, presents clinico-pathological correlations. The electrocardiograms recorded by a direct writer, three leads simultaneously, and apparently the same apparatus for all the records used in selecting the illustrations give a satisfactory uniformity which facilitates reading these records. Considering that these electrocardiograms were recorded in children, the baselines are remarkably straight. The clinical and anatomical information related to the electrocardiograms, although brief, is composed with studied economy of words, giving much information by inference to the reader who is familiar with the subject. One could not ask for more in an atlas. The reader who proves to be unfamiliar with a given item would be inspired to learn about it from other sources. The pages are necessarily of the larger variety to accommodate the electrocardiograms. The format and paper are very good. The list of "specimens" includes a wide variety of items from the range of normal and the more common congenital and rheumatic types of heart disease, to a number of rare ones. This book is a good atlas of paediatric electrocardiography.

(Continued on advertising page 27)

NEWS & VIEWS

ON THE ECONOMICS OF MEDICINE

Prepared
by the Department of
Medical Economics.
The Canadian
Medical Association

NUMBER 7

Our sources of information are private communications and published comments in medical journals and the lay press. These are usually reliable but incorrect quotation or interpretation is always possible.

Saskatchewan

As the June 8 election date approaches, political parties in Saskatchewan stepped up the tempo of their activities. Pronouncements on the CCF-proposed medical care plan are more frequent.

Progressive Conservative Leader Pederson announced that his party fully endorses the principle of comprehensive medical care. He indicated that his party differs from the CCF government on administration and implementation of such a program. (1)

Liberal Leader Thatcher accused the CCF of "peddling untruths" about the Liberal party's stand on the proposed prepaid medical care plan. Indicating that "what the people want, they will be able to get under a Liberal government", he stated that, if elected, the Liberal party would examine the various plans and the comparative costs after the heat of the election had subsided. Then the facts would be laid before the public and a plebiscite held. (2)

Premier Douglas admitted that his government would have a problem deciding whether or not the people want the CCF medical care plan if the party is returned to office with less than half the popular vote. In 1956 the CCF received 45 per cent of the vote. (3)

The Canadian Medical Association Executive Committee discussed the medical problems with representatives of the Saskatchewan Division at a recent meeting. The CMA Executive Committee issued the following statement:

"Dr. J. F. C. Anderson, Past President of The Canadian Medical Association, on behalf of the Saskatchewan Division and its President, Dr. A. M. J. Davies, reported to a meeting of the Executive of the C.M.A. in Toronto on April 23rd. He stated that very serious concern was currently being expressed in Saskatchewan as a result of the Saskatchewan Government's statement that compulsory medical care insurance would be imposed on the residents of Saskatchewan, if it was returned at the next Election.

Dr. E. Kirk Lyon, Deputy to the President of The Canadian Medical Association, said that Canadian medicine is still in favour of

(over)

NEWS AND VIEWS on the economics of medicine (cont'd)

its long established policy of giving every consideration to proposals for prepaid medical care - provided they are in the public interest and genuinely aimed at improving the health of the people. Dr. Lyon issued a warning that the C.M.A. was opposed to any approach that would interfere with the rights of the public to a personal medical service provided by a free profession.

The C.M.A. Executive commended the Saskatchewan representatives for their excellent interpretation and presentation to their Government of the principles accepted by the C.M.A. regarding prepaid health care, and indicated to them that the medical profession across Canada heartily endorses the position taken by the doctors of Saskatchewan." (4)

Britain

The Government has announced in the House of Commons that it is prepared to accept the recommendations of the Royal Commission on Remuneration (see News and Views No. 4, March 5, 1960) as a whole, provided that the profession is ready to accept them on the same basis.

Acceptance of the Government's offer does not commit the profession to acceptance of merit awards to general practitioners (a highly controversial matter) but it does indicate acceptance of a body to keep medical remuneration under review on the basis proposed by the Commission.

Correspondence between the profession and the Government has clarified that members of this review body must be acceptable to the profession and that the profession would have reasonable, if indirect, access to such a body. (5)

REFERENCES:

- (1) Saskatoon Star Phoenix, May 18, 1960.
- (2) Saskatoon Star Phoenix, May 19, 1960.
- (3) Regina Leader-Post, May 19, 1960.
- (4) C.M.A. News Release, April 25, 1960.
- (5) Private Correspondence.

FORTHCOMING MEETINGS

CANADA

CANADIAN FEDERATION OF BIOLOGICAL SOCIETIES (comprising the Canadian Physiological Society, the Pharmacological Society of Canada, the Canadian Association of Anatomists and the Canadian Biochemical Society), Third Annual Meeting, Winnipeg, Man. (Dr. E. H. Bensley, Honorary Secretary, Montreal General Hospital, 1650 Cedar Ave., Montreal 25, Que.) June 8-10, 1960.

THE SOCIETY OF OBSTETRICIANS AND GYNÆCOLOGISTS OF CANADA, Annual Meeting, Jasper Park Lodge, Jasper, Alta. (Dr. F. P. McInnis, Secretary, 280 Bloor St. West, Toronto 5, Ont.) June 9-12, 1960.

CANADIAN OTOLARYNGOLOGICAL SOCIETY (SOCIÉTÉ CANADIENNE D'OTOLARYNGOLOGIE), Annual Meeting, Jasper Park Lodge, Jasper National Park, Alberta. (Dr. Donald M. MacRae, Secretary, 324 Spring Garden Road, Halifax, N.S.) June 10-12, 1960.

CANADIAN OPHTHALMOLOGICAL SOCIETY (SOCIÉTÉ CANADIENNE D'OPHTALMOLOGIE), Annual Meeting, Jasper Park Lodge, Jasper National Park, Alberta. (Dr. R. G. C. Kelly, Secretary, 90 St. Clair Avenue West, Toronto 7, Ont.) June 13-15, 1960.

CANADIAN MEDICAL ASSOCIATION, 93rd Annual Meeting, Banff, Alberta. (Dr. A. D. Kelly, General Secretary, C.M.A. House, 150 St. George Street, Toronto 5, Ont.) June 13-17, 1960.

CANADIAN DIETETIC ASSOCIATION, 25th National Congress, Montreal, Que. (Miss Claire Dalmé, M.N.S., Chairman, Publicity Committee, Institute of Dietetics and Nutrition, University of Montreal, P.O. Box 6128, Montreal, Que.) June 14-16, 1960.

CANADIAN SOCIETY OF INTERNAL MEDICINE, Annual Business Meeting, Banff Springs Hotel, Banff, Alta. (Dr. Victor O. Hertzman, Secretary, 1744 West Broadway, Vancouver 9, B.C.) June 17, 1960.

CANADIAN TUBERCULOSIS ASSOCIATION, 60th Annual Meeting, Ottawa, Ont. (Dr. G. J. Wherrett, Executive Secretary, 265 Elgin St., Ottawa, Ont.) June 27-30, 1960.

CANADIAN UROLOGICAL ASSOCIATION, Annual Meeting, Banff Springs Hotel, Banff, Alta. (Dr. David Swartz, President, 332-404 Graham Ave., Winnipeg 1, Man.) July 1-3, 1960.

PACIFIC DERMATOLOGIC ASSOCIATION, Annual Meeting, Victoria, B.C. (Dr. Edward J. Ringrose, Secretary-Treasurer, 2636 Telegraph Ave., Berkeley 4, Cal., U.S.A.) September 1-4, 1960.

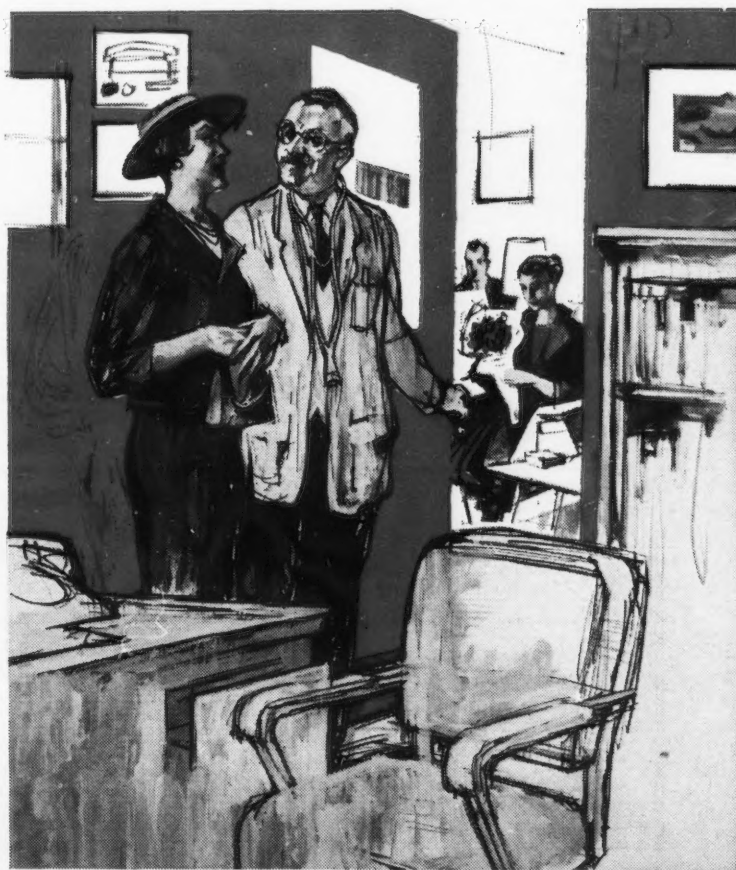
2ND WORLD CONGRESS OF THE WORLD FEDERATION OF SOCIETIES OF ANÆSTHESIOLOGISTS, Toronto, Ont. (Dr. R. A. Gordon, Chairman of Organizing Committee, 178 St. George Street, Toronto 5, Ont.) September 4-10, 1960.

ONTARIO PUBLIC HEALTH ASSOCIATION, Annual Meeting, Toronto, Ont. (Dr. G. K. Martin, Secretary-Treasurer, O.P.H.A., Room 405, 67 College St., Toronto, Ont.) October 3-5, 1960.

CANADIAN HEART ASSOCIATION AND NATIONAL HEART FOUNDATION OF CANADA, Joint Annual Meeting, Toronto, Ont. (For information write: Dr. John B. Armstrong, National Heart Foundation, 501 Yonge St., Toronto 5, Ont.) November 30 to December 3, 1960.

UNITED STATES

INTER-SOCIETY CYTOLOGY COUNCIL, Annual Scientific Meeting, Chicago, Ill. (Dr. Paul A. Younge, Secretary-Treasurer, 1101 Beacon St., Brookline 46, Mass.) September 23-25, 1960.



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References: Authors should limit references to published work to the minimum necessary for guidance to readers wishing to study the subject further. They should not quote articles they have never seen. Except in review articles, the maximum number of references should not be more than 25. References should be numbered in the text and should be set out in a numbered list at the end of the article, thus:

1. DOAKES, J.: *M. J. Kamchatka*, 1: 2, 1955, giving in order: (1) Author's name and initials in capitals. Where more than three authors are concerned in an article, only the first should be named, with *et al.* as reference to the others. (2) Quarterly Cumulative Index Medicus abbreviation of journal name. (3) Volume number. (4) Page number. (5) Year.

References to books should be set out as follows:

PICKWICK, S., *Textbook of Medicine*, Jones and Jones, London, 1st ed., p. 30, 1955.

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Classified advertisements must be at the office of the Journal not later than three weeks prior to date of issue.

Miscellaneous

PROFEX—X RAY UNIT 300 mm A 100 Kv complete with rotating anode tube. Hand-driven, counter-balanced table with fluoroscopic screen and bucky. Diaphragmatic and wall-bucky stand. Used short time. Reasonable. Reply to Box 814, CMA Journal, 150 St. George St., Toronto 5, Ontario.

Office Space

OFFICE with waiting room, examining room and laboratory for sublet from June or July 1960 to April 30, 1961. Located on Sherbrooke St. W., Montreal with convenient parking. Moderate rental. Receptionist service included on request. For further details please write to Box 823, CMA Journal, 150 St. George St., Toronto 5, Ontario.

COMPLETELY EQUIPPED MODERN OFFICE for general practice one block from large shopping center in Hamilton, Ontario. Will rent or sell with or without equipment. Available July 1, 1960. Write Dr. R. Richter, 46 Sherman Ave. S., Hamilton, Ontario.

NEW RESIDENCE AND SUITE for sale or rent. Spacious office, examination room, reception room, washroom, also a large residence. Don Mills district, prominent address, main thoroughfare. Ample parking. Please phone PL. 7-3516.

DOCTOR'S SUITE available July 1, 1960. Waiting room, operating room, recovery room. St. Clair and Avenue Road in Toronto. Parking available. \$100 monthly. For further information phone HU. 9-4533.

Positions Wanted

DERMATOLOGIST.—McGill graduate, 1956 American board eligible, desires position with established specialist or group for 1 to 2 years. Available September 1960. Reply Dr. B. Gordon, New York Skin and Cancer Unit, 330 Second Ave., New York 3, N.Y.

GENERAL SURGEON 35, Canadian and American trained, fellowship eligible, would like to associate with another surgeon, clinic or group. Address replies to Box 792, CMA Journal, 150 St. George St., Toronto 5, Ontario.

EUROPEAN 41, 5 years' salaried G.P. in Canada, wishes position as associate or assistant with view to partnership. Available immediately until July 31 for one month locum tenens which could be trial period for permanent association or locum tenens only. Reply to Box 824, CMA Journal, 150 St. George St., Toronto 5, Ontario.

LOCUM AVAILABLE, July or August, married, four children, own car, Saskatchewan licence, for general practice duties. Reply to Box 825, CMA Journal, 150 St. George St., Toronto 5, Ontario.

CANADIAN GRADUATE, 30, married, three years' post-graduate in internal medicine, presently in the United Kingdom, would like position in industry or small group. Adaptable. Some experience in general practice. Available January, 1961. Replies to Box 826, CMA Journal, 150 St. George St., Toronto 5, Ontario.

BOOK REVIEWS

(Continued from page 1198)

THE PSYCHIATRIC NURSE IN THE GENERAL HOSPITAL. Mary A. Tudbury. 83 pp. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1959. \$3.75.

Miss Tudbury has presented a report of a study which was done in a psychiatric unit in a general hospital. The study was concerned with the role of the psychiatric nurse expert, and its purpose was to find out the role of the present psychiatric nurse in this unit; what the nurses, attendants and aides were doing and how the role of the nurses compared with the defined role of the psychiatric nurse expert. It was also thought that by actually introducing this expert into the position in a designated unit, it would help to reveal its value and enable the nursing personnel to gain knowledge regarding preparation for this type of position.

A 20-bed unit for psychiatric patients in a general hospital was selected for the study. The majority of the patients on this unit were transfers from other wards within the hospital, with varying types of mental illness exclusive of the major psychoses. As this unit was a specific centre for psychotherapeutic research, physiotherapeutic forms of treatment were not used.

In her presentation of the study, Miss Tudbury has used the case method.

The introduction of Miss Knudson (research fellow) to the position of psychiatric nurse expert on the unit used for the study, enabled her to study and evaluate many aspects of psychiatric nursing with complete freedom from administrative responsibilities. The study of the present staff revealed that 59% of the nurse's time was occupied with administrative functions, and 29% in educational activities and interpersonal relationships.

Miss Tudbury has brought out in her report the need for the psychiatric nurse to be able to spend more time with the patient if she is going to be able to meet his emotional needs. An understanding of the dynamics of behaviour as expressed by the patient's attitude requires that the nurse have knowledge of mental illnesses, the causative factors, an

awareness of herself and her reactions. This knowledge is also essential if she is to be effective in working with patients as they progress from illness to health and in creating a therapeutic environment.

This book should be very useful as it presents material pertinent to psychiatric nursing very concisely and in an interesting way. Its title

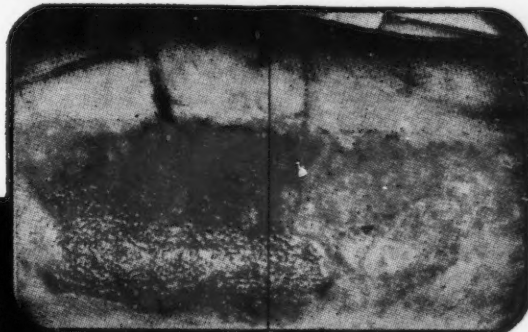
is rather misleading; one would expect to find more about the psychiatric nurse in the general hospital setting. The understanding gained of human behaviour, the skills developed in communication, and the ability to participate as an active member of the team would apply to a well-prepared psychiatric nurse, not an expert.

(Continued on page 29)

Versatile topical

FURACIN CREAM

in a new
bactericidal
form



Skin graft donor site after 2 weeks' treatment with . .

petrolatum gauze—
still largely
granulation tissue

FURACIN gauze—
completely epithelialized

TOPICAL—For postoperative anorectal use, as well as for application to general infected areas.

INDICATIONS:

INTRAVAGINAL—Before and after: delivery-gynecologic surgery—irradiation and office procedures—to prevent or treat infection and facilitate healing of the cervix and vagina.

For bacterial (nonspecific) vaginitis and cervicitis.

COMPOSITION—Furacin (brand of nitrofurazone) 0.2% in a fine cream base, water-miscible and self-emulsifying in body fluids.

advantages

- (1) Wide-range bactericide effective in exudates and organic debris.
- (2) Does not induce significant bacterial resistance, nor encourage monilial overgrowth.
- (3) Nontoxic to healing tissue.
- (4) Slightly acid pH (5.0) helps restore normal physiologic balance in the vagina.
- (5) Odorless and esthetically pleasing.

HOW SUPPLIED—Tubes of 3 oz., with or without plastic plunger-type vaginal applicator.

DOSAGE AND ADMINISTRATION—Intravaginally, the usual dosage is 1 applicatorful, morning and night. Topically—apply to infected areas.

References (1) Weiner, A. L., and Fixler, Z. C.: J.A.M.A. 169:346, 1959. (2) Nesbitt, R. E. L., Jr.: Investigator's report to the Medical Department, Eaton Laboratories. (3) Jennett, R. J.: Investigators report to the Medical Department, Eaton Laboratories.

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GUELPH



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an all-round defence against



in all its phases

HYPON is a new non codeine analgesic for the relief of transient and chronic pain associated with dysmenorrhoea, rheumatism and neuralgia. Its analgesic properties are provided by N. acetyl paraminophenol, acetylsalicylic acid and phenacetin.

Side effects of depression and constipation associated with long term administration of analgesics are countered by the inclusion of caffeine and a minimal dose of phenolphthalein.

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HYPON TABLETS

FORMULA: Each tablet contains:

Acetylsalicylic Acid.....	200 mg.
N. acetyl paraminophenol.....	60 mg.
Phenacetin.....	200 mg.
Caffeine.....	8 mg.
Phenolphthalein.....	5 mg.

Dose: One tablet three times daily or as prescribed.
Presented in: Packs of 10, 50 and 300 tablets.

BOOK REVIEWS

(Continued from page 27)

CINEFLUOROGRAPHY. Proceedings of the First Annual Symposium on Cinefluorography, sponsored by the Department of Radiology, University of Rochester School of Medicine and Dentistry. Edited by G. H. S. Ramsey and others. 266 pp. Illust. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1960. \$13.00.

The text is a compilation of papers presented at the First Symposium on Cinefluorography held at the University of Rochester, N.Y., in November 1958. The history and development of cinefluorography are outlined. The physics and optics associated with the various methods of image intensification are briefly discussed. The problems with regard to the choice of cameras, film and processing methods are indicated. The various methods are compared from the standpoint of radiation exposure and patient safety. Some indications as to the present research trends with regard to improvements in the existing methods are also reported.

MEDICAL NEWS in Brief

(Continued from page 1173)

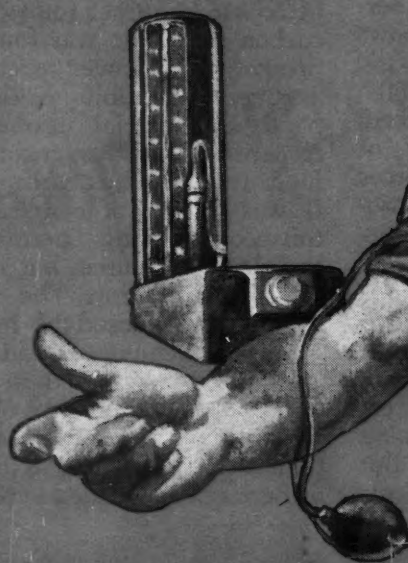
THE COMPLEXITY OF SUBMARINE TRAVELLING

With all the present intense concentration on overcoming obstacles to space travel, there still is fascination in the medical problems that attend travel in the opposite medium, that is, in prolonged submarine immersion and cruising. This is not a form of locomotion which is likely to involve many people (nor it may be said is the other) but it still is extremely interesting to learn how complex the maintenance of living conditions becomes in a submarine, especially when there is prolonged submersion.

The subject is well dealt with by Lt. Commander J. H. Ebersole (*New England J. Med.*, 262: 599, 1960) in discussing "The New Dimensions of Submarine Medicine", beginning with a dramatic comparison between living conditions in submarines only 14 years ago and those of the modern nuclear-powered ships. It would be even more impressive if the comparison were extended back to the submarine of World War I. The point, however, is to empha-

(Continued on page 30)

unexcelled
combination of
effectiveness
and safety...



RAUTRACTYL

Squibb Benzhydroflumethiazide (Naturetin) and Rauwolfia Serpentina Whole Root (Raudixin) with Potassium Chloride

Rautracyl combines Naturetin, the best diuretic available in effectiveness, safety and potency with Raudixin, the cornerstone of antihypertensive therapy.

- effective in all degrees of essential hypertension — mild, moderate and severe.
- increased urine output with minimal alterations in electrolyte balance — urine composition remains more nearly physiological.
- supplementary potassium provides added protection against potassium loss during long-term therapy or when treating patients unusually prone to hypokalemia.
- unexcelled effectiveness and safety because it produces the highest degree of natriuresis and water diuresis with reduced kaliuresis.



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SUPPLY: Rautracyl-2 Tablets (capsule-shaped) containing 2 mg. Benzhydroflumethiazide (Naturetin) and 50 mg. Rauwolfia Serpentina Whole Root (Raudixin) with 400 mg. Potassium Chloride; bottles of 100. Rautracyl-4 Tablets (capsule-shaped) containing 4 mg. Benzhydroflumethiazide (Naturetin) and 50 mg. Rauwolfia Serpentina Whole Root (Raudixin) with 400 mg. Potassium Chloride; bottles of 100.

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MEDICAL NEWS in brief

(Continued from page 29)

size the revolutionary change in the capacity of the submarine to remain submerged for long periods. In 1944 complete submergence for only about 24 hours at a time could be maintained, and that only with great difficulty. In 1958 the nuclear-powered submarine *Seawolf* with a large crew remained under water steadily for 60 days in comfort, and apparently could have continued for longer quite easily.

In reading Commander Ebersole's account one hardly knows whether to wonder more at the exacting conditions under which the older submarine crews worked, or the extraordinary infinity of mechanical and chemical sources which had to be considered in producing the almost normal living conditions on the *Seawolf*.

The major factor in the change is, of course, the use of nuclear power instead of electric batteries, whose very limited power did not permit of air conditioning, for example, without greatly shortening the length of the submersion. But even so, there were many problems

to be overcome. Radiation control curiously enough never became a major difficulty: actually radiation was turned to good account in some degree in dealing with aerosols. The disposal of CO_2 called for the development of "scrubbers" which picked up the gas from the air by treatment with amines and discharged it overboard. But the amine is a chemical of great volatility and is toxic, and this called for leak-proof piping and continual vigilance.

The nuclear submarine is free of course of diesel fumes, but still carbon monoxide was found to be present in the lower reaction compartment. Possibly oxidation of paint and special insulation was responsible for this, together with high temperatures and radiation. It was known of course that the tobacco smoking permitted on board was a source, but its effects were allowed for. The CO was eventually disposed of by special burners which converted it to CO_2 .

The gas freon used in refrigeration was another source of trouble. In ordinary household air-conditioning units this gas is contained in hermetically sealed systems, but

on the submarine this sealing is not possible as there must be access for repair. Absolute freedom from leaks has never been attained although very special attention has reduced it to a safe minimum. Freon is relatively non-toxic, but under heat it decomposes into hydrochloric acid, chlorine, hydrofluoric acid, and fluorine, with serious effects both on health and on equipment. The vicious circle formed is a good instance of the interdependence of mechanical factors; the freon escapes, is picked up by the CO burner and promptly is broken down into the halides; these damage the burner itself, which eventually fails to pick up the freon, which then enters the air and builds up to danger point when it is broken down by the many other heat sources such as flame photometers, electric heating apparatus, and cigarettes.

Another unexpected source of trouble was found to be the cleaning fluids and the oil-base paints used in the traditional naval cleaning and painting as well as the

(Continued on page 36)



SHE'S FREE FROM SYMPTOMS AND SIDE EFFECTS ON MEDROL*

The sufferer with seasonal pollinosis symptom-free under therapy with Medrol will rarely present, even to the practiced clinical eye, any of the disturbing changes in appearance, behavior or metabolism often associated with corticotherapy.

Fewer and less serious side reactions on therapeutically effective doses is the hallmark of Medrol.

Supplied as 2 and 4 mg. tablets in bottles of 30 and 100.

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Announcing

'ACTIFED'

Decongestant / Antihistamine

THE POTENTIATED DECONGESTANT



provides symptomatic relief of
nasal congestion and rhinor-
rhea of allergic or infectious

origin Many patients whose symptoms are inadequately controlled by decongestants or antihistamines alone respond promptly and favorably to 'ACTIFED'.

'ACTIFED' contains:	in each Tablet	in each tsp. Syrup
'Actidil' brand Triprolidine Hydrochloride	2.5 mg.	1.25 mg.
'Sudafed' brand Pseudoephedrine Hydrochloride	60 mg.	30 mg.

**safe and effective for patients
of all ages suffering from upper
respiratory tract congestion**

DOSAGE			} three times daily
	TABLETS	SYRUP (5 cc. tsp.)	
Adults and older children	1	2	
Children 4 months to 6 years of age	½	1	
Infants through 3 months	—	½	



BURROUGHS WELLCOME & CO. (CANADA) LTD., Montreal

MEDICAL NEWS in brief*(Continued from page 30)*

liquid deck waxes. All these produced aliphatic hydrocarbons with toxic capacities.

These are by no means all the things that have to be thought of; final mention, however, may be made of unexpectedly finding benzene in the form of an adhesive in the leather-working kits supplied to the crew for recreation. This had not been marked in any way to show its nature and of course formed a potential hazard.

How successfully these and many other hurdles were surmounted is all strikingly shown by the *Sea-wolf's* historic trip of 15,000 miles in two months of complete submersion with a crew of 116 officers and men.

THE SOCIETY OF NUCLEAR MEDICINE

The Seventh Annual Meeting of the Society of Nuclear Medicine will be held at the Stanley Hotel, Estes Park, Colorado, June 22-25, 1960. Over seventy speakers will present new scientific information covering every phase of research, medicine and surgery as it concerns the use of nuclear phenomena in the diagnosis and treatment of disease. Special emphasis will be given to the diagnosis and treatment of thyroid disease, the therapeutic use of radioisotopes and "tools of the trade".

The meeting is open to all physicians, veterinarians, nurses, physicists, technicians and other scientists working with, or interested in utilizing, radioisotopes in the health field. There is a non-member registration fee of \$5.00. Registration forms and copies of the program may be secured by writing to Mr. Samuel N. Turiel, Administrator, The Society of Nuclear Medicine, 430 N. Michigan Avenue, Chicago 11, Illinois.

INTERNATIONAL SYMPOSIUM ON THE EXTRAPYRAMIDAL SYSTEM AND NEUROLEPTICS

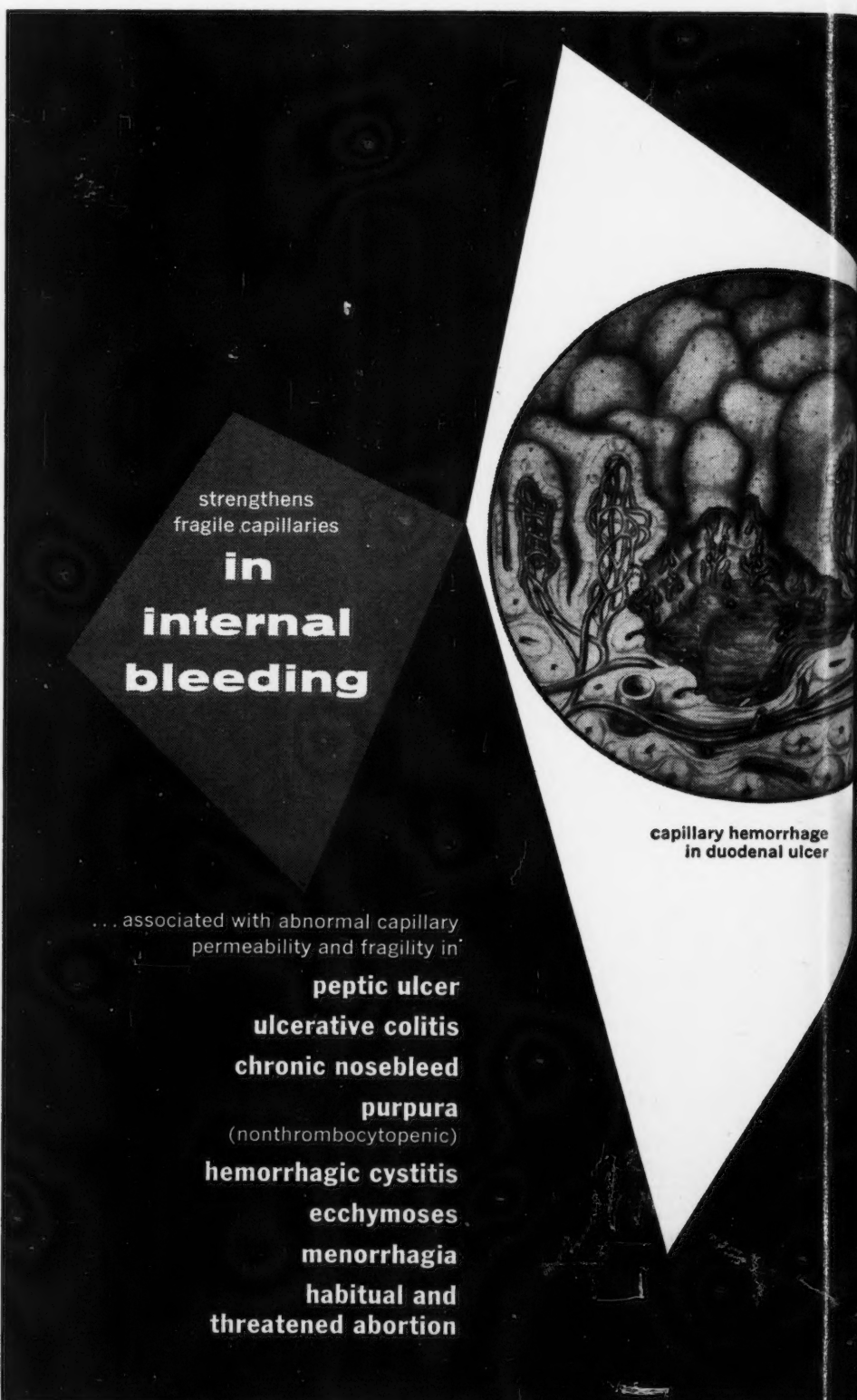
The Department of Psychiatry of the University of Montreal is organizing an international symposium on "The Extrapyraxidal System and Neuroleptics" to be held at the University of Montreal

on November 17, 18 and 19, 1960. This symposium will permit an exchange of ideas among research workers interested in this subject from the point of view of anatomy, physiology, neurosurgery and psychiatry. Admission to the symposium will be unrestricted but participation will be by invitation only. The symposium will be held with the co-operation of the ten Canadian provinces, the United States and several European coun-

tries. There will be two official languages, English and French, with simultaneous translation. For information, write to: Dr. Jean-Marc Bordeleau, Department of Psychiatry, University of Montreal, Montreal, Quebec.

THE KINGSTON MEDICAL SERVICES CENTRE

The following extracts are taken from an address given by Dr. J. A.



strengthens
fragile capillaries

**in
internal
bleeding**

capillary hemorrhage
in duodenal ulcer

... associated with abnormal capillary
permeability and fragility in

peptic ulcer

ulcerative colitis

chronic nosebleed

purpura
(nonthrombocytopenic)

hemorrhagic cystitis

ecchymoses

menorrhagia

**habitual and
threatened abortion**

MacFarlane, Dean of the Faculty of Medicine at the University of Toronto, on October 9, 1959, on the occasion of the opening of the Kingston Medical Services Centre at Kingston, Ontario.

"Nearly seven years ago, Dr. Hall, the President of the University of Western Ontario, chaired a special committee with terms of reference from the then Minister of Defence to investigate the possibilities of reorganization of the

Medical Services, and in particular to seek ways and means of further integration, and the maintenance of a service that would be highly efficient and, as such, an attractive career to young Canadian doctors.

"That committee made several recommendations, which were subsequently approved by the Government. One of the most important was for the establishment of three hospital centres — centres which would combine the most modern

facilities for treatment with opportunities for training personnel of the Medical Services at all levels. The report stressed the importance of building such centres in close proximity to medical schools, and the establishment of the closest relations with the schools concerned.

"At the time of the establishment of the Canadian Forces Medical Council, an organization which resulted from another recommendation of the Hall Committee, the D.G.M.S. (Army) had under consideration the plans for a new military hospital at Kingston. The Council early in its deliberations decided that here in association with the Medical School of Queen's University there should be established one of the three new Medical Service units, a modern health and treatment centre to be staffed by specialists and doctors and nursing sisters from the three services, and meeting the needs of all three services in the surrounding area. . .

"Although the original plans for this hospital were being put on the drawing board by the Army even before the inception of the Council, the proposed unit fitted easily into its integration plans, and we are gratified to see today in physical form this very solid and substantial result, the first National Defence Medical Centre, an important unit in the Canadian Forces Medical Service. We are very happy that Queen's University has agreed to an arrangement whereby it will also be an integral part of the teaching facilities of that great and historic foundation. . ."

"Those who are responsible for the plans of the new Medical Service have the courage and confidence to proceed with a unified Medical Service. To serve the day-to-day health needs of the present three arms of our defence, to collaborate in research with the Defence Research Board, to make plans for the contingency of national involvement in total war along with our civilian colleagues but having some solid grounds for hoping the major war will be averted, to plan for and supply the health needs of a unified, highly efficient, intelligent, well-trained Canadian Defence Force — this I see to be the future role of an equally efficient and highly trained Medical Service. This new centre will, I am sure, play an important

(Continued on page 42)

duo- CVP

(double strength CVP)

water-soluble citrus bioflavonoid
compound (200 mg.) with ascorbic acid
(200 mg.), per capsule

Duo-C.V.P. helps diminish increased capillary permeability, fragility, and resultant bleeding by acting to maintain the integrity of the intercellular ground substance (cement) of capillary walls. Duo-C.V.P. is the original and exclusive water-soluble citrus bioflavonoid complex. Readily absorbed and utilized, duo-C.V.P. is relatively free (due to special processing) of hesperidin, naringin and other comparatively insoluble and inactive flavonoids found in citrus.

duo-C.V.P. is available in bottles of 50, 100, 500 and 1000 capsules.

also available: duo-C.V.P. with vitamin K capsules
C.V.P. capsules
C.V.P. with vitamin K syrup

arlington-funk laboratories, division
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1452 Drummond Street, Montreal, Quebec

NEW

the unique
anorexic agent
free of
CNS
stimulation

for the . . .
cardiac/hypertensive obese

New Tenuate provides an anorexic effect which assures appetite inhibition, free of CNS stimulation.¹⁻⁷ ECG studies⁸ prove Tenuate does not affect heart rate, blood pressure, pulse or respiration.

Weight loss with Tenuate averages 1.5 pounds per week.^{3,4} Resultant weight loss, by reducing the cardiac load, improves prognosis . . . and, frequently when hypertensives lose weight, blood pressure drops. Thus Tenuate fulfills an important medical need . . . weight loss in cardiac/hypertensive patients.

PROOF—SAFETY—ECG EVIDENCE⁸

Human I.V. Studies with Tenuate 10 mg., IV equiv. of 100 mg. oral dose (4 times recommended dose)

Patients	Sex	Age	Diagnosis	Blood Pressure		ECG	
				Before Inj.	After Inj.*	Control	After Inj.
E. M.	F	62	Diabetes mellitus. A.S.H.D., compensated. Obesity, postmenopausal.	125/54	116/52	Sinus rhythm. Nonspecific myocardial changes.	No change
F. S.	M	67	A.S.H.D., mild hypertension. Early congestive cardiac failure.	175/90	175/90	Sinus rhythm. Early LVH.	No change
M. A.	F	68	Essential hypertension. Degenerative osteoarthritis. Obesity.	207/104	194/98	Sinus rhythm. Normal tracing.	No change
S. G.	M	30	Normal subject.	126/74	122/78	Sinus rhythm. Normal tracing.	No change
D. A.	M	33	Normal subject.	112/80	121/90	Sinus rhythm. Normal tracing.	No change

*This represents the averages of the readings taken at 30-second and 1-minute intervals for 5 minutes prior to injection and 5 minutes after injection of the drug. The amount of fluctuation was considered insignificant.

as it calms anxiety!

Smooth, balanced action lifts depression as it calms anxiety... rapidly and safely

Balances the mood—no “seesaw” effect of amphetamine-barbiturates and energizers. While amphetamines and energizers may stimulate the patient—they often aggravate anxiety and tension.

And although amphetamine-barbiturate combinations may counteract excessive stimulation—they often deepen depression.

In contrast to such “seesaw” effects, Deprol’s smooth, *balanced* action lifts depression as it calms anxiety—both at the same time.

Acts swiftly—the patient often feels better, sleeps better, within a few days. Unlike the delayed action of most other antidepressant drugs, which may take two to six weeks to bring results, Deprol relieves the patient quickly—often within a few days. Thus, the expense to the patient of long-term drug therapy can be avoided.

Acts safely—no danger of liver damage. Deprol does not produce liver damage, hypotension, psychotic reactions or changes in sexual function—frequently reported with other antidepressant drugs.

Bibliography (13 clinical studies, 858 patients): 1. Alexander, L. (35 patients): Chemotherapy of depression—Use of meprobamate combined with benactyzine (2-diethylaminoethyl benzilate) hydrochloride. J.A.M.A. 166:1019, March 1, 1958. 2. Bateman, J. C. and Carlton, H. N. (50 patients): Meprobamate and benactyzine hydrochloride (Deprol) as adjunctive therapy for patients with advanced cancer. Antibiotic Med. & Clin. Therapy 6:648, Nov. 1959. 3. Beerman, H. M. (44 patients): The treatment of depression with meprobamate and benactyzine hydrochloride. Western Med. 1:10, March 1960. 4. Bell, J. L., Tauber, H., Santy, A. and Pulito, F. (77 patients): Treatment of depressive states in office practice. Dis. Nerv. System 20:263, June 1959. 5. Breitner, C. (31 patients): On mental depressions. Dis. Nerv. System 20:142, (Section Two), May 1959. 6. Gordon, P. E. (50 patients): Deprol in the treatment of depression. Dis. Nerv. System 21:215, April 1960. 7. Landman, M. E. (50 patients): Clinical trial of a new antidepressive agent. J. M. Soc. New Jersey. In press, 1960. 8. McClure, C. W., Papas, P. N., Speare, G. S., Palmer, E., Slattery, J. J., Konefal, S. H., Henken, B. S., Wood, C. A. and Ceresia, G. B. (128 patients): Treatment of depression—New techniques and therapy. Am. Pract. & Digest Treat. 10:1525, Sept. 1959. 9. Pennington, V. M. (135 patients): Meprobamate-benactyzine (Deprol) in the treatment of chronic brain syndrome, schizophrenia and senility. J. Am. Geriatrics Soc. 7:656, Aug. 1959. 10. Rickels, K. and Ewing, J. H. (35 patients): Deprol in depressive conditions. Dis. Nerv. System 20:364, (Section One), Aug. 1959. 11. Ruchwarger, A. (87 patients): Use of Deprol (meprobamate combined with benactyzine hydrochloride) in the office treatment of depression. M. Ann. District of Columbia 28:438, Aug. 1959. 12. Settel, E. (52 patients): Treatment of depression in the elderly with a meprobamate-benactyzine hydrochloride combination. Antibiotic Med. & Clin. Therapy 7:28, Jan. 1960. 13. Splitter, S. R. (84 patients): Treatment of the anxious patient in general practice. J. Clin. & Exper. Psychopath. In press, April-June 1960.

Dosage: Usual starting dose is 1 tablet q.i.d. When necessary, this dose may be gradually increased up to 3 tablets q.i.d.

Composition: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.
Supplied: Bottles of 50 light-pink, scored tablets. Write for literature and samples.



WALLACE LABORATORIES / Toronto, Ontario

Deprol[†]

†TRADE-MARK

MEDICAL NEWS in brief

(Continued from page 37)

part in the future of the Service, and I would like to pay tribute to all those who have been responsible for the plans for its development, and the actual design and building of this very attractive and functional Medical Centre."

1er COLLOQUE DE MEDECINE SUB- AQUATIQUE

Le Club Alpin Sous-Marin de Cannes organise du 15 au 19 juin 1960 le premier colloque international de médecine sub-aquatique. Cette manifestation tiendra ses assises au Palais des Festivals sur la Croisette à Cannes.

Les différentes séances traiteront des sujets suivants: Les accidents de plongée libre—Causes et prévention. Les accidents de décompression—Causes, prévention et traitement. Ivresse des grandes profondeurs. Problèmes posés par la plongée à l'oxygène et aux mélanges gazeux.

Pour tous renseignements s'adresser au Comité d'Organisation du Colloque, Club Alpin Sous-Marin, 10, Place Commandant Lamy, Cannes (A.M.), France.

WHY NOT AN INTERNATIONAL BIOLOGICAL YEAR?

A proposal has been made for the formation of an International Biological Year (IBY) to help in solving the many major problems associated with biology. The suggestion was first made at a Washington conference on the Control of Insects of Medical Importance, when it was thought that an International Ecological Year might be organized, the general idea being "to manipulate natural biological systems by fitting new organisms into man-made niches". Apparently, however, exploration of this only served to emphasize the "unfathomed gaps in existing ecological and taxonomic knowledge, lack of coordination, and lags in communication".

On further consideration, it has become apparent that no effort of

such a nature can be justified unless all biology is included. It seems, however, that there is at least some body of belief that an IBY would be enormously profitable once it could be brought into being; but the problems of its organization are so vast that for the moment no specific proposals have been put forward. It is felt that if the proposition has inherent merit, the size of the problem should not be disheartening. Its very size might serve as a challenge which would bring out support and make it more feasible than a succession of smaller projects. Naturally, the International Geophysical Year just completed comes to mind, but the focusing of co-ordinated biological work might be even more difficult than were the arrangements for the IGY. The proposal for the formation of such a Year was first made by Dr. John R. Olive, assistant executive director of the American Institute of Biological Sciences, when he was summing up the results of a Biological Control Conference. The problems which would come before such a body are ex-

(Continued on page 47)



SHE'S FREE FROM SYMPTOMS AND SIDE EFFECTS ON MEDROL*

The sufferer with seasonal pollinosis symptom-free under therapy with Medrol will rarely present, even to the practiced clinical eye, any of the disturbing changes in appearance, behavior or metabolism often associated with corticotherapy. Fewer and less serious side reactions on therapeutically effective doses is the hallmark of Medrol.

Supplied as 2 and 4 mg. tablets in bottles of 30 and 100.

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*Trademark, Methylprednisolone, Upjohn

MEDICAL NEWS in brief

(Continued from page 42)

tremely numerous and important, for example, pest controls versus wild-life, sewage disposal, algæ-pollution control, nutrition, population pressure, etc., etc. It may be years even before such an organization comes into being but it is encouraging to find that the thought at least is there and that it may be developed.

POISON-PRODUCING
PLANKTON

Reports were made recently at the New York Academy of Sciences by Schantz, Burke and Shilo of their studies on the toxins of *Gonyaulax catenella*, a single-celled plankton plant which is known to appear at certain times on the sea coasts of North America. When it is eaten by mussels and other shellfish, these become extremely poisonous for human beings. Apparently Dr. Shilo shows that this plankton appeared about 10 years ago in the waters of the carp farms in Israel. These farms are a valuable source of fish food for the Israelis. The studies are being directed towards the control of this plankton. It can be killed by the constant application of ammonium salts to the carp ponds, but this is an expensive and lengthy procedure. By finding out more about the plant's nutritional needs, Dr. Shilo hopes to discover ways of preventing its growth.

SECOND INTERNATIONAL
CONGRESS OF
NEUROLOGICAL SURGERY

The Second International Congress of Neurological Surgery, sponsored by the World Federation of Neurosurgical Societies, will take place at the Statler-Hilton Hotel, Washington, D.C., on October 14 to 20, 1961. The scientific program will consist of four symposia to be presented Monday, Tuesday, Thursday and Friday mornings and voluntary papers to be presented in the afternoons of the same four days. The names of speakers who will discuss the symposia topics will be announced later. The following topics have been selected for the

(Continued on page 49)

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(1) Ford R.V., Rosen, David J. (in Press)
(2) Report 15251 to the Squibb Institute for Medical Research

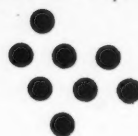


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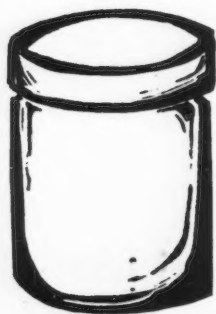
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treats their acne while they wash

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FOR OILY ACNE

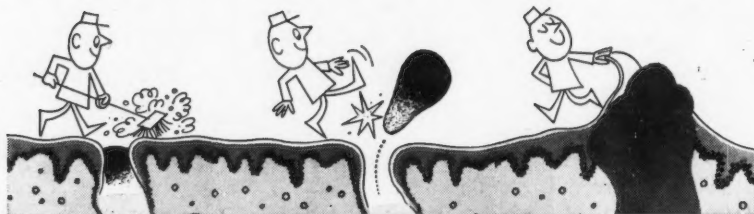
For therapeutic washing in acne when the skin is very oily and blackheads abound. Fostex Cream provides maximum drying action to degrease the skin and help remove blackheads. It is also used as a therapeutic shampoo in associated dandruff and oily scalp.

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degreases the skin helps remove blackheads dries and peels the skin

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MEDICAL NEWS in brief

(Continued from page 47)

morning symposia: (1) radioactivity in heavy radiation particles in neurosurgery; (2) space-occupying intracranial lesions; (3) re-evaluation of surgery in the treatment of pain, and (4) biology of the nervous system, and hydrocephalus. Further information may be obtained from the Secretary General, Dr. Bronson S. Ray, 525 East 68th Street, New York 21, N.Y.

FIRST INTERNATIONAL SYMPOSIUM OF CYBERNETIC MEDICINE

The first International Symposium of Cybernetic Medicine, organized by the International Society of Cybernetic Medicine, will be held in Naples, Italy, October 2-4, 1960, under the presidency of Prof. Aldo Masturzo of Naples University. The general theme will be "The introduction of cybernetic methods in modern medicine". In addition to the scientific program, trips are being arranged to Pompei, Sorrento and

other points of interest near Naples. Those wishing to participate in the Symposium should notify the Secretary (Professor Fenato Vinciguerra, Via Roma 348, Naples, Italy) not later than June 30, forwarding the registration fee of ten dollars and submitting the titles of their communications.

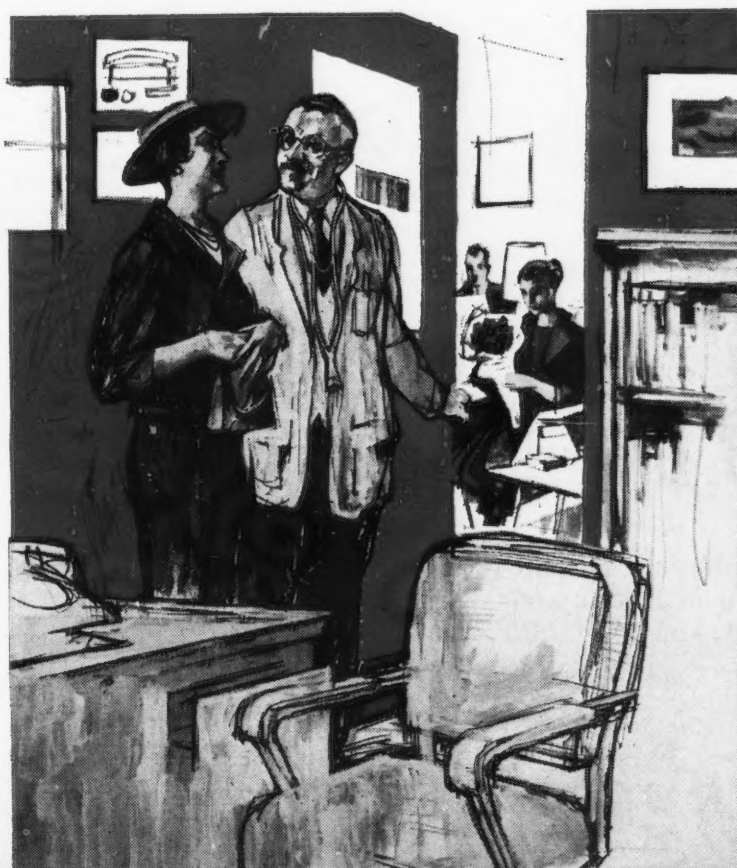
SEWAGE LAGOONS

Sewage treatment has currently been receiving accelerated and critical interest in regard to its significance as a public health hazard or nuisance, its importance in controlling gross pollution of watercourses, and finally its cost in terms of both capital expenditure and operation. A type of waste stabilization pond known as a sewage lagoon, a shallow open pond for the treatment of raw sewage, has been in use for over 10 years in the state of North Dakota. Kay (*Canad. J. Pub. Health*, 51: 108, 1960) states that the acceptance of sewage lagoons in Manitoba has been the most important single public health development

in the post-war years. In this article he outlines the effectiveness, the functioning, and the planning and operation of lagoons.

One of the more significant problems encountered was the matter of admixture of industrial waste with domestic sewage, a situation that could arise in any small community interested in attracting industries. This difficulty can be met, but industrial waste lagooning should be the responsibility of the user agency. The problem of odour control, at different periods of the year, can be most satisfactorily solved by use of sodium nitrate, at minimal cost.

Single cell domestic sewage lagooning provides at least the equivalent of primary treatment at a capital expenditure of above half that for a standard plant and an annual operating and maintenance cost of a small fraction of the usual allowance for this purpose. The problem of sludge treatment and disposal is, in most if not all installations, non-existent.



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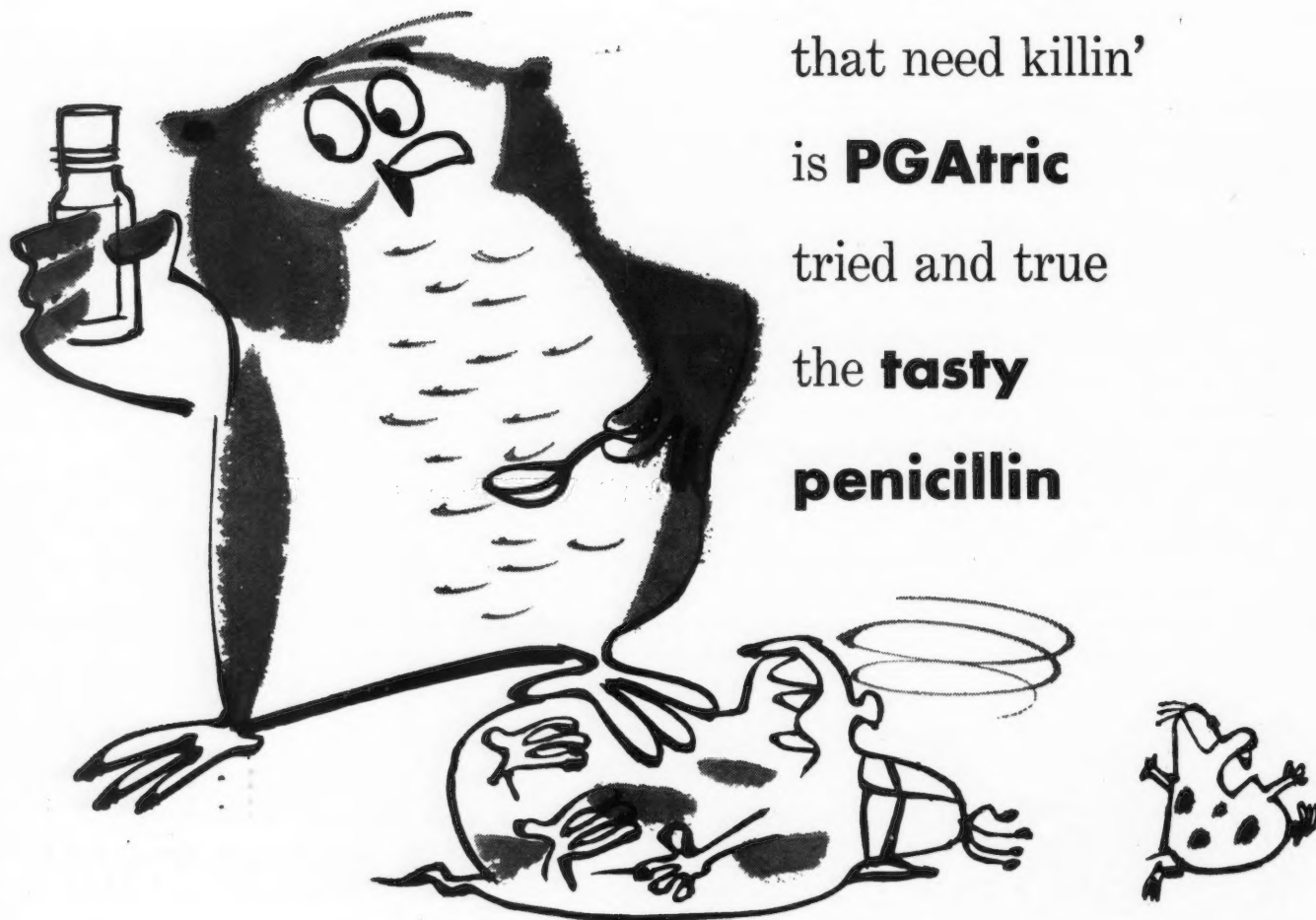
The sufferer with seasonal pollinosis symptom-free under therapy with Medrol will rarely present, even to the practiced clinical eye, any of the disturbing changes in appearance, behavior or metabolism often associated with corticotherapy. Fewer and less serious side reactions on therapeutically effective doses is the hallmark of Medrol.

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